Considered 02/19/04 WC

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=> fil wpids
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=> d que l35
L1        63839 SEA FILE=WPIDS ABB=ON  PLU=ON  OLIGONUCLEOTID? OR ?OLIGO (2W)
                NUCLEOTIDE OR DNA
L2        32138 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (S) (PROTEIN OR ?PEPTIDE?)
L3         1026 SEA FILE=WPIDS ABB=ON  PLU=ON  L2 (S) CONJUGAT?
L6          570 SEA FILE=WPIDS ABB=ON  PLU=ON  L3 AND ?LINK?
L7           10 SEA FILE=WPIDS ABB=ON  PLU=ON  SULFO (2W) (SMCC OR EMCS OR
                GMBS OR KMUS OR MBS OR SIAB OR SMPB OR LS SMPT OR SMPT OR SVSB
                OR SIACX OR SIA OR SIAXX OR NPIA)
L8          729 SEA FILE=WPIDS ABB=ON  PLU=ON  (SMCC OR EMCS OR GMBS OR KMUS
                OR MBS OR SIAB OR SMPB OR LS SMPT OR SMPT OR SVSB OR SIACX OR
                SIA OR SIAXX OR NPIA)
L9            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L6 AND L7
L10           1 SEA FILE=WPIDS ABB=ON  PLU=ON  L3 AND L7
L11           5 SEA FILE=WPIDS ABB=ON  PLU=ON  L8 AND L3
L12       48973 SEA FILE=WPIDS ABB=ON  PLU=ON  (AMINO OR AMINE) (3A) (GRP# OR
                GROUP#)
L13         469 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (S) L12
L14         267 SEA FILE=WPIDS ABB=ON  PLU=ON  L13 AND L2
L15           1 SEA FILE=WPIDS ABB=ON  PLU=ON  L14 AND L8
L16         151 SEA FILE=WPIDS ABB=ON  PLU=ON  L14 AND ?LINK?
L17        6769 SEA FILE=WPIDS ABB=ON  PLU=ON  (THIO### OR SULF###) (3A) (GRP#
                OR GROUP#)
L18          21 SEA FILE=WPIDS ABB=ON  PLU=ON  L16 AND L17
L19           6 SEA FILE=WPIDS ABB=ON  PLU=ON  L3 AND L18
L20          44 SEA FILE=WPIDS ABB=ON  PLU=ON  L13 AND L3
L21          30 SEA FILE=WPIDS ABB=ON  PLU=ON  L20 AND ?LINK?
L22           6 SEA FILE=WPIDS ABB=ON  PLU=ON  L21 AND L17
L23           6 SEA FILE=WPIDS ABB=ON  PLU=ON  L19 OR L22
L24          10 SEA FILE=WPIDS ABB=ON  PLU=ON  L23 OR L15 OR L11 OR L10 OR L9
L25          26 SEA FILE=WPIDS ABB=ON  PLU=ON  L8 AND L1
L26           6 SEA FILE=WPIDS ABB=ON  PLU=ON  L25 AND CONJUG?
L27          15 SEA FILE=WPIDS ABB=ON  PLU=ON  L25 AND ?LINK?
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L28 17 SEA FILE=WPIDS ABB=ON PLU=ON L26 OR L27
L29 12 SEA FILE=WPIDS ABB=ON PLU=ON L28 NOT L24
L35 22 SEA FILE=WPIDS ABB=ON PLU=ON L24 OR L29 OR L28

=> d .wp 1-22

L35 ANSWER 1 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-008897 [01] WPIDS
DNC C2004-002242
TI New molecular carrier useful for introducing substance e.g. pharmacological agent or genetic material into cells, comprising central multivalent core to which several adduct molecules are bonded.
DC A96 B04 B05 B07 D16
IN CHU, Y L; LAI, W; LI, F Q; QIU, J; ZHU, S
PA (CHUY-I) CHU Y L; (LAIW-I) LAI W; (LIFQ-I) LI F Q; (QIUJ-I) QIU J; (ZHUS-I) ZHU S
CYC 1
PI US 2003068379 A1 20030410 (200401)* 30p
ADT US 2003068379 A1 Provisional US 2001-310492P 20010808, US 2002-137355 20020503
PRAI US 2001-310492P 20010808; US 2002-137355 20020503
AB US2003068379 A UPAB: 20040102
NOVELTY - A molecular carrier (I) comprising a central multivalent core to which several adduct molecules are bonded, is new.

DETAILED DESCRIPTION - A molecular carrier (I) of formula (F1), (F2) and (F3), comprising a central multivalent core to which several adduct molecules are bonded, is new.

Adduct = residue of an amino acid;
n = integer of 2 or greater;
m = 0 or a positive integer; and
p = positive integer.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmacological agent/molecular carrier complex (II) comprising (I) and a pharmacological agent that is associated with at least one of the adduct moieties;

(2) a genetic material/molecular carrier complex (III) comprising (I) and genetic material which is associated with one of the adduct moieties;

(3) forming (M1) a molecular carrier by covalently bonding several adduct molecules to a central multivalent core molecule by reacting a nucleophilic group on each adduct molecule with an electrophilic group on the multivalent core molecule, where the multivalent core molecule comprises electrophilic groups;

(4) forming (M2) a molecular carrier comprising covalently bonding several adduct molecules to a central multivalent core molecule by reacting an electrophilic group on each adduct molecule with a nucleophilic group on the multivalent core molecule, where the multivalent core molecule comprises nucleophilic groups, and is chosen from benzene-tetramine, a tri(carboxymethyl)amine, ((Lys)2Lys)3-(TFA), where TFA is a tri-functional amine, diethylaminetriamine, triethylenetetramine, Tris(hydroxymethyl)aminomethane (TRIS), and NH2((CH2)nNH)m(CH2)n NH2, where n and m are integers which may vary throughout the molecule;

(5) a molecular carrier made by (M1) or (M2), and (II) and (III) produced by (M1); and

(6) (II) and (III) comprising a molecular carrier made by (M2).

USE - (I) is useful for introducing a substance into cells by incubating cell(s) with (I) associated with a pharmacological agent (e.g. non-**peptide** drugs, **proteins**, **peptides**, steroids or hormones) or a genetic material, for in vivo transfection of cells, comprising administering (I) associated with a pharmacological

agent or a genetic material, into the cells. (I) is also useful for performing gene therapy by administering a gene therapy agent comprising (I) associated with a genetic material such as an expression vector containing a **DNA** segment encoding a **protein** or an anti-sense **oligonucleotide** to a human or animal. The gene therapy agent (I) is useful for improving the pharmacokinetic profile of a pharmacological agent. (I) may be used to **conjugate** pharmacological agent(s).

ADVANTAGE - (I) provides a drug delivery vehicle that can improve the pharmacokinetics or pharmacological agent.

Dwg.0/15

TECH UPTX: 20040102

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Molecular Carrier: The molecular carrier is of formula (a).

Preferred Complex: (II) further comprises a second pharmacological agent associated with at least one of the adduct moieties, which is different from the first pharmacological agent. The adduct moiety comprises an enzyme labile bond (preferably a disulfide bond) that is labile to intracellular enzymes, digestive enzymes or serum enzymes. (II) further comprises a receptor, a receptor ligand or a receptor binding **protein** associated with one of the adduct moieties.

The pharmacological agent is chosen from non-**peptide** drugs, **proteins**, **peptides**, steroids and hormones, a **peptide** antigen capable of eliciting an immune response, an opiate **peptide**, a leutinizing hormone releasing hormone (LHRH) antagonist, paclitaxel, or an angiogenic agent which inhibits or stimulates angiogenesis. The molecular carrier comprises maleimide group(s) and the pharmacological agent comprises a **thiol group** and is covalently associated with the molecular carrier by reaction of the **thiol group** on the pharmacological agent with the maleimide group on the molecular carrier.

(II) is dispersed in a solution as an emulsion or suspension, or the molecular carrier is immobilized to a solid support. In (III), the molecular carrier comprises positively charged surface functional group(s), and the genetic material is ionically associated with the molecular carrier through the charged groups. The molecular carrier preferably comprises the residue of a polyfunctional **amine**, where the **amine groups** are protonated to form the charged groups. The genetic material is chosen from **DNA**, RNA, **oligonucleotides**, and nucleic acids. Some of the adduct molecules are bonded to other adduct molecules.

Preferred Method: In (M1), the multivalent core molecule is a polyfunctional-carboxylic acid, succinic acid or ethylene diamine tetraacetic acid (EDTA). The nucleophilic group on each adduct molecule is an **amino group.** The adduct molecules comprise glutamic acid, aspartic acid or its adducts. The adduct molecules preferably comprise tetra-ester of Glu(Glu)2, octa-ester of (Glu(Glu(Glu)2)2), hexadeca-ester of (Glu(Glu(Glu-(Glu)2)2)2) or esters of higher order adducts of glutamic acid. The adduct molecules comprise glutamic acid ester or aspartic acid ester adducts, and the method further comprises a step of hydrolyzing the ester groups on the adduct molecules to the corresponding carboxylic acid groups.

(M1) further comprises:

(i) reacting a first N-substituted glutamic or aspartic acid with 2 equivalents of a glutamic or aspartic acid di-ester and de-protecting the **amine groups** on the first glutamic or aspartic acid to form a first glutamic or aspartic acid di-ester adduct;

(ii) optionally reacting a second N-substituted glutamic or aspartic acid with 2 equivalents of first glutamic or aspartic acid di-ester and de-protecting the **amine groups** on the second glutamic

or aspartic acid to form a second glutamic or aspartic acid di-ester adduct;
(iii) optionally reacting a third N-substituted glutamic or aspartic acid with 2 equivalents of the second glutamic or aspartic acid di-ester adduct and de-protecting the **amine group** on the third
glutamic or aspartic acid to form a third glutamic or aspartic acid di-ester adduct; and
where the adduct molecules covalently bonded to the multivalent core comprise the first, second and/or third glutamic or aspartic acid di-ester adducts. The adduct molecules comprise enzyme labile **linkages**, preferably disulfide **linkages.**
(M1) further comprises a step of associating a pharmacological agent with the molecular carrier, by covalently bonding the agent to the carrier. The step also involves associating a receptor or a receptor ligand with the carrier. The reacting step is conducted in the presence of a catalyst e.g. carbodiimide, preferably 1-ethyl-3-(3- dimethylaminopropyl)-carbodiimide (EDC) or N,N-dicyclohexyl-carbodiimide (DCC). The molecular carrier comprises carboxylic acid surface functional groups, and the method further involves:
(a) reacting surface functional carboxylic acid group(s) on the molecular carrier with a polyamine to provide **amine** surface functional **groups**, and ionically complexing genetic material to the **amine** surface functional **groups**; or
(b) reacting a compound comprising a maleimide group and a carboxylic acid reactive functional group with the surface functional group(s) to provide maleimide surface functional group(s), and covalently attaching a pharmacological agent to the molecular carrier by reacting a **thiol group** on the pharmacological agent with the maleimide group(s) on the molecular carrier.
The pharmacological agent is preferably a **peptide** containing a cysteine residue. The core molecule is chosen from benzene-tetracarboxylic acid, cyclopentane-tetracarboxylic acid, butane-tetracarboxylic acid, ethylenediamine tetralkylcarboxylic acid, ethylene glycol-bis(beta-amino-ethyl ether)-N,N,N',N'-tetraacetic acid, 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid, spermidine pentaacetic acid, spermine-hexaacetic acid, ((COOH)CH2)2 N(CH2)3 NCH2COOH(CH2)3 NH2, and (COOH)CH2)2 N(CH2)3 NCH2 COOH (CH2)3 NH2, and (COOH)CH2N(CH2)3 NCH2 COOH(CH2)2 NH2.
In (M2), the adduct molecules comprise lysine or arginine residues, and the method further comprises:
(i) reacting a first lysine or arginine ester molecule with 2 equivalents of lysine or arginine and hydrolyzing the ester group on the first lysine or arginine to a carboxylic acid to form a first lysine or arginine adduct;
(ii) optionally reacting a second lysine or arginine ester with 2 equivalents of the first lysine or arginine adduct and hydrolyzing the ester group on the second lysine or arginine ester to a carboxylic acid to form a second lysine or arginine adduct;
(iii) optionally reacting a third lysine or arginine ester with 2 equivalents of the second lysine or arginine adduct and hydrolyzing the ester group on the third lysine or arginine ester to a carboxylic acid to form a third lysine or arginine adduct; and
where the adduct molecules covalently bonded to the multivalent core comprise the first, second and/or third lysine or arginine adducts.

L35 ANSWER 2 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-697456 [66] WPIDS
CR 1997-332441 [30]
DNC C2003-191750
TI New homogeneous prodrug **conjugate** containing hepatic ligand for delivery of pathogen-specific oligomer useful for treating liver

infections or cancer.
DC B04 C03 D16
IN DEAMOND, S; DUFF, R; ROBY, C; TS'O, P O P; ZHOU, Y
PA (CELL-N) CELL WORKS INC; (UYJO) UNIV JOHNS HOPKINS
CYC 100
PI WO 2003067209 A2 20030814 (200366)* EN 107p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2003067209 A2 WO 2002-US19908 20020621
PRAI US 2001-888164 20010622
AB WO2003067209 A UPAB: 20031014

NOVELTY - Homogeneous **conjugate** (I) comprising a hepatic ligand, bifunctional **linker** and biologically stable oligomer that binds to a sequence in a hepatic virus or pathogen and is released from the **conjugate** by hydrolysis or reduction, is new.

DETAILED DESCRIPTION - Homogeneous **conjugate** of formula A-L-P (I) comprising a hepatic ligand that specifically binds to a hepatic receptor; bifunctional **linker** that is covalently **linked** to the hepatic ligand and biologically stable oligomer that binds to an (encapsidation) sequence in a hepatic virus or pathogen and is released from the **conjugate** by hydrolysis or reduction of biochemical **linkage**(s)and contains internucleotide **linkages** resistant to enzymatic hydrolysis or biodegradation upon release from the **conjugate.**

A = hepatic ligand, specific for a hepatic receptor that facilitates entry of (I) into receptor-bearing cells;

L = bifunctional **linker** covalently **linked** to A and P in regiospecific manner; and

P = biologically stable oligomer that binds to an encapsidation sequence of a hepatic virus.

P is released from the **conjugate** following hydrolysis or reduction of at least one specific biochemical **linkage.** It contains internucleotide **linkages** resistant to enzymatic hydrolysis or biodegradation on release from the **conjugate.**

An INDEPENDENT CLAIM is also included for synthesis and radiolabeling of (I), where the oligomer is an **oligonucleotide**, analog, or oligonucleoside.

ACTIVITY - Virucide; Hepatotropic; Antiinflammatory; Cytostatic; Antiparasitic.

When 10 micro M of the **conjugate** (Ia) was administered to confluent monolayers of HepG2 2.2.15 cells, the amount of hepatitis B virions (pg/106 cells) formed was only about 200; compared to about 1400 in the absence of (Ia).

Tyr-Glu-Glu-(ahGalNAc)-3-**SMCC**-5'-AAAGCCACCCAAGGCA (Ia)

SMCC = hydroxysuccinimidyl-4-(N-methylmaleimido)cyclohexyl carboxylate;

MECHANISM OF ACTION - Antisense inhibition of protein synthesis. No biological data given.

USE - (I) are used as prodrugs for delivering therapeutic oligomers to liver cells, for treatment, in human or veterinary medicine, of viral or parasitic diseases or hepatic cancer, most especially infection by hepatitis B, C or D viruses.

ADVANTAGE - The A-L component provides ligand-directed, receptor-mediated deliver of (I) to hepatocytes, where the active agent (P) is released.

Dwg.0/20
TECH UPTX: 20031014
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: The oligomer is an **oligonucleotide** or analog, or oligonucleoside that targets a hepatitis virus and binds to an RNA sequence in the preS1 open reading frame. Particularly it includes deoxyribose methylphosphonate , phosphorothioate or phosphodiester internucleotide **linkages**, optionally also 2'-O-methyl ribose residues, or any combination of them. Three **oligonucleotide** sequences are specified, most preferred is S3 which targets the unpaired loop of the encapsidation site of the hepatitis B virus pregenome.
AAAGCCACCCAAGGCA (S3)
The most preferred **conjugate** is Tyr-Glu-Glu-(ahGalNAc)-3-**SMCC**-5'-AAAGCCACCCAAGGCA
SMCC = hydroxysuccinimidyl-4-(N-methylmaleimido)cyclohexyl carboxylate.
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (claimed): Synthesizing the **conjugate** comprises:
(a) forming an A-L construct;
(b) purifying the A-L construct to over 95 % homogeneity and removing any unreacted L;
(c) modifying P to form a thiol-modified oligomer;
(d) purifying the thiol-modified oligomer under degassed conditions;
(e) reacting the A-L construct and the thiol oligomer in a two-component **conjugation** reaction under degassed conditions, where the reaction is performed using excess amounts of the ligand scaffold or the thiol modified oligomer to form the A-L -P **conjugate**; and
(f) purifying the A-L-P **conjugate** by size-exclusion chromatography (SEC).
Alternatively, L, with a terminal disulfide residue, is attached to P during its solid-phase synthesis, the product is purified, reduced to thiol and then reacted with A. In this case, A-L-P is purified by electrophoresis or HPLC and the modified oligomer is purified by SEC.
A typical process for radiolabeling the **conjugate** is:
(a) adding the tracer unit 5'-T-3'-ps-3'-T-ps-T-5' to the 3'-end of P, during synthesis;
(b) enzymatic phosphorylation to incorporate radiolabeled phosphate (using polynucleotide kinase and labeled adenosine triphosphate); and
(c) chemically modifying the radioactive phosphate by **conjugation** to an amine, to protect it against enzymatic degradation.
Alternatively, radiolabeling the **conjugate** comprises:
(a) adding a disulfide-terminated **linker** to the 5' end of P and adding the tracer unit 5'-T-3'-ps-3'-T-ps-T-5' to the 3'-end of P, during synthesis;
(b) purifying the disulfide and tracer containing P;
(c) reducing the disulfide functional group to a thiol group to form a thiol modified P;
(d) purifying the thiol-modified P using SEC to remove unreacted reagent;
(e) **conjugating** an A-L construct to the purified thiol-modified P;
(f) enzymatically phosphorylating the tracer unit to incorporate radiolabeled phosphate (using polynucleotide kinase and labeled adenosine triphosphate); and
(g) chemically modifying the radioactive phosphate by **conjugation** to an amine, to protect it against enzymatic degradation.

L35 ANSWER 3 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-568888 [53] WPIDS
DNN N2003-452509 DNC C2003-153306
TI Detection of an enzyme useful in drug discovery involves measuring a

change in deflection of a microcantilever having a substrate for the enzyme.

DC A89 B04 D16 P42 S03
IN BOTTOMLEY, L A; GHOSH, M; SAUL, R; SHEN, S
PA (PROT-N) PROTIVERIS INC
CYC 100
PI WO 2003023363 A2 20030320 (200353)* EN 16p
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003068655 A1 20030410 (200353)
ADT WO 2003023363 A2 WO 2002-US28920 20020911; US 2003068655 A1 US 2001-951131 20010912
PRAI US 2001-951131 20010912
AB WO2003023363 A UPAB: 20030820

NOVELTY - Detecting (M1) an enzyme by:

(a) depositing a coating material (c1) on a first surface of at least one microcantilever (m1);

(b) adding at least one substrate (s1) (capable of interacting with the enzyme or the substance) to (c1);

(c) exposing (m1) with (s1) to a sample; and

(d) measuring a deflection of (m1), where the deflection indicates a presence of the enzyme in the sample, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) detection (M1') of an associating substance in a sample, where the substance binds to (s1) and the detection involves at least one (m1) configured to be responsive to a micro-force, involving steps (1), (2), exposing (m1) with (s1) to the sample, and measuring a resulting free surface energy change, where the energy change indicates binding to (s1) by the associating substance in the sample;

(2) a method (M2) of screening for an inhibitor of an enzyme having (s1) on (m1) having a coating involving:

(a) adding (s1) (which is capable of interacting with the enzyme) to a first side of a first (m1) and a second (m1);

(b) exposing the first (m1) with (s1) to a sample containing a candidate inhibitor and the enzyme; and

(c) measuring a deflection of the first (m1) in comparison to a deflection of the second (m1) identically exposed to the enzyme and in the absence of the candidate inhibitor; and

(3) an apparatus to measure a micro-force generated by an interaction between the enzyme and a bio-material (preferably enzymatic substrate or enzymatic pseudo-substrate), comprising at least one (m1), a coating material deposited on a first surface of (m1), a bio-material attached to the coating material and at least one interaction cell containing (m1) housed in a micro-fluidics device for receiving a sample, where the detection of the micro-force is indicated by deflection of (m1) due to the presence of the enzyme in the sample.

USE - For detecting an enzyme associated with a medical condition (e.g. genetic defect, Fabry disease, Gaucher disease, Tay-Sachs disease, Lesch-Nyhan disease, mannosidosis disease, X-**linked** glomerular disease and mucopolysaccharidosis, cancer (e.g. brain, liver, pancreas, lung, prostate, and breast) in a vertebrate animal; the presence of infectious agent e.g. virus, bacterium, fungus, protozoan and helminth) (all claimed). Also useful in proteomics, drug discovery, medical research, medical, veterinary, dental diagnostics, forensics and military

applications, in research; for detection and analysis of binding activities of enzymes and enzyme-like proteins.

ADVANTAGE - The methods detect the interaction between enzymes and their substrates.

Dwg.0/4

TECH UPTX: 20030820

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Step (b) of M1 involves adding at least one biomaterial or a drug; and designing (m1) for detecting the enzyme. The deflection is caused by a change in stress on the surface of (m1).

Preferred Enzyme: The enzyme is hydrolase (preferably protease), oxidoreductase, transferase, lyase, ligase, kinase, phosphatase, endopeptidase, exopeptidase, restriction endonuclease, exonuclease or polymerase, or a component (c2). The protease is a metalloprotease or serine protease. The transferase is glycosyl transferase, glutathione S-transferase, an acetyl transferase or a **DNA** methyl transferase. The lyase is polysaccharide lyase, a 3-hydroxy-3-methylglutaryl Coenzyme A lyase, argininosuccinate lyase or an isocitrate lyase. The oxidoreductase is hydroxylamine oxidoreductase, glyphosphate oxidoreductase, quinine oxidoreductase, ubiquinone oxidoreductase or a protein disulfide oxidoreductase. When present in the sample, the enzyme is substantially purified. (c2) is prostate specific antigen or collagenase.

Preferred Components: In (M1'), the associating substance is an enzyme, which binds (s1) and fails to dissociate, and has no activity on (s1). In (M1'), (s1) is a non-cleavable pseudo-substrate, several bio-materials or an inhibitor of enzymatic activity. In the apparatus, the bio-material comprises an enzymatic pseudo-substrate.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: In step 4), the deflection is measured by optical, electron tunneling, capacitive, piezoelectric or piezoresistive methods (preferably by optical method including a laser). The method (M1) further involves analyzing the deflection of (m1) as a function of a time parameter determined from the time of exposing (m1) to the sample by using a microprocessor; prior to adding (s1) to the first surface, reacting the first surface with a bifunctional cross-**linker**, where the bifunctional cross-**linker** is capable of further reacting with (s1). The microprocessor compares, calculates and stores the deflection of (m1) as a function of the time parameter. The analyzing step additionally involves analyzing a parameter selected from concentration of enzyme, concentration of substrate, presence of a cofactor and presence of an inhibitor.

Preferred Apparatus: (m1) has a length of about 100 - 750 microm, width of 20 - 300 microm and thickness of 0.1 - 10 microm. In (M2), the first (m1) is located in a first interaction cell and the second (m1) is located in a second interaction cell of a micro-fluidics device. A third (m1) is located in a third interaction cell and a fourth (m1) is located in a fourth interaction cell, which are exposed to a different concentration of enzyme than the first and second cells; or different samples containing candidate inhibitors than the candidate in the first interaction cell. In (M1), (m1) is in a block array containing several (m1). The apparatus is disposable and reusable.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The biofunctional cross-**linker** is dithiobis(succinimido undecanoate (DSU), long chain succinimido-6-(3-(2-pyridyldithio)-propionamido)hexanoate (LCSPDP), succinimidyl-6-(3-(2-pyridyldithio)-propionamido)hexanoate (SPDP), or m-maleimidobenzoyl-N-hydroxysuccinimide ester (**MBS**) (preferably (DSU)).

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: In (M1), the substance is a nucleic acid, protein, lipid, hydrocarbon or a polysaccharide. In (M1), the sample is a biological fluid selected from cell lysate, culture medium, spent medium, animal extract, plant extract; bodily fluid from a vertebrate animal (preferably mammal e.g. human). The bodily fluid is blood, lymph, tissue fluid, urine, bile, sweat, synovial fluid, amniotic fluid, abdominal fluid, pericardial fluid, pleural fluid, cerebrospinal fluid, gastric juice, intestinal juice, joint cavity fluid, tears or nasal discharge. In (M1'), the associating substance is a binding protein, cofactor, receptor ligand, antibody, polysaccharide, lipid, nucleic acid or steroid.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Method: In M1, step (a) further involves depositing metal(s), where a first layer of chromium and a second layer of gold, or a first layer of titanium and second layer of gold is deposited.
Preferred Metal: The metal is amalgam, an alloy; or a component (c1). (c1) is aluminum, copper, gold, chromium, titanium or silver (preferably gold). (m1) has a second surface selected from aluminum oxide, iridium oxide, silicon, silicon oxide, silicon nitride, tantalum pentaoxide or plastic polymer. In the apparatus, the second surface of (m1) is silicon, silicon nitride, other silicon compounds, metal compounds, gallium arsenide, germanium, germanium dioxide, glass, zinc oxide, diamond, quartz, palladium or plastic polymer. In the apparatus, the coating material is (c1).

L35 ANSWER 4 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-543481 [52] WPIDS
DNC C2003-147566
TI New hybridization substrate for use in a complementarity test, comprises **DNA** strands having a double-strand portion and a single-strand portion, that are immobilized on the surface of a substrate.
DC B04 D16
IN HARA, M; ITO, E; NAKAJIMA, K; NAKAMURA, F
PA (RIKE) RIKEN KK; (HARA-I) HARA M; (ITOE-I) ITO E; (NAKA-I) NAKAJIMA K; (NAKA-I) NAKAMURA F
CYC 32
PI EP 1279434 A2 20030129 (200352)* EN 10p
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
JP 2003043037 A 20030213 (200352) 9p
US 2003022227 A1 20030130 (200352)
ADT EP 1279434 A2 EP 2002-16613 20020725; JP 2003043037 A JP 2001-228374 20010727; US 2003022227 A1 US 2002-205363 20020726
PRAI JP 2001-228374 20010727
AB EP 1279434 A UPAB: 20030813
NOVELTY - A hybridization substrate (I), comprises **DNA** strands having a double-strand and single-strand portion immobilized on a substrate surface, where the double-strand portion of the **DNA** strands is immobilized on the substrate surface.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the manufacture (M) of (I), comprising contacting **DNA** strands having a double-strand and single-strand portion, and a thiol group present on the terminal of the double-strand portion, with the metal surface of a metal substrate or a substrate having a metal coating, to immobilize the **DNA** strands on the metal surface.
USE - (I) Is useful in a complementarity test, in which target **DNA** is contacted with the surface of (I) on which **DNA** strands have been immobilized to test for complementarity between the target **DNA** and the single-strand portion of the **DNA**

strands having a double-strand portion and a single-strand portion. The presence or absence of hybridization between the target **DNA** and the single-strand portion of the **DNA** strands is detected by a surface plasmon resonance method or quartz crystal microbarance (QCM) method. The target **DNA** is a **DNA** having a fluorescent label and hybridization with the single-strand portion of the **DNA** strand is detected using fluorescence or a radioisotope (RI), and target **DNA** comprising a mismatched nucleic acid base is also detected (claimed).

ADVANTAGE - (I) Is cost-effective.

DESCRIPTION OF DRAWING(S) - The figure shows the scheme of preparing thiolated **DNA** oligomer, and the hybridization process.

Dwg.1/4

TECH UPTX: 20030813

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Substrate: The substrate is a metal substrate or a substrate having a metal coating, or a glass or silicon substrate, and the **DNA** strands have been immobilized on the metal surface of the substrate, using a sulfur atom. The number of nucleic acids of the double-strand and single-strand portion ranges from 10 - 80 and 20 - 90, respectively. In addition to the **DNA** strands having a double-stranded and a single-stranded portion, **DNA** strands having only a double-strand portion have been further immobilized on the surface of the substrate. The immobilization ratio of the **DNA** strands having a double- and single-strand portion, to **DNA** strands having only a double-strand portion ranges from 99:1 - 1:99. The metal substrate or metal coating is made of gold.

Preferred Method: The surface of a glass or silicon substrate is surface treated with a hetero bifunctional **crosslinking** agent to immobilize the **DNA** strands on the surface. Contacting with the **DNA** strands is conducted in the presence of bivalent ions e.g. magnesium ions. The hetero bifunctional **crosslinking** agent is selected from succinimidyl-4-(maleimidophenyl)butyrate (**SMPB**), m-maleimidobenzoyl-N-hydroxysuccinimidoester (**MBS**), succinimidyl-4-(maleimidomethyl)cyclohexane-1-carboxylate (**SMCC**), N-(gamma-maleimidobutyloxy)succinimidoester (**GMBS**), m-maleimidopropionic acid-N-hydroxysuccinimidoester (MPS), and N-succinimidyl(4-iodoacetyl)amino benzoate (**SIAB**).

L35 ANSWER 5 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-441258 [41] WPIDS
DNC C2003-116747
TI Producing **oligonucleotide-protein conjugate** by contacting **oligonucleotide** having **amino group** with **linker** having two **groups** reactive with **amino** and **thiol groups**, contacting **conjugate** formed with **protein** having **thiol group.**
DC B04 D16
IN FAROOQUI, F; REDDY, P M
PA (FARO-I) FAROOQUI F; (REDD-I) REDDY P M; (BECI) BECKMAN COULTER INC
CYC 28
PI WO 2003035830 A2 20030501 (200341)* EN 32p
RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
W: AU CA CN DE GB JP
US 2003092901 A1 20030515 (200341)
ADT WO 2003035830 A2 WO 2002-US32317 20021011; US 2003092901 A1 US 2001-32592 20011024
PRAI US 2001-32592 20011024
AB WO2003035830 A UPAB: 20030630

this appears

NOVELTY - Producing (M) **oligonucleotide-protein conjugate** (C1), comprising contacting **oligonucleotide** having an **amino group** (AG) with a heterofunctional **linker** (HL) having first group (G1) reactive with AG and second **group** (G2) reactive with **thiol group** (TG), where G1 becomes bonded to AG to form **oligonucleotide**-HL **conjugate** (C2), and contacting (C2) with **protein** having TG, where TG becomes bonded to G2 to form C1, is new.

DETAILED DESCRIPTION - Producing (M) an **oligonucleotide-protein conjugate**, involves contacting an **oligonucleotide** having an **amino group** with a heterofunctional **linker**, where the **linker** has a first **group** reactive with the **amino group** and a second **group** reactive with a **thiol group**, where the contacting is performed under conditions sufficient to permit the first group of the **linker** to become bonded to the **amino group** of the **oligonucleotide**, to form an **oligonucleotide**-heterofunctional **linker conjugate**, and contacting the **oligonucleotide**-heterofunctional **linker conjugate** with a **protein** having a **thiol group** reactive with the second group of the **linker**, where the contacting is performed under conditions sufficient to permit the **thiol group** of the **protein** to become bonded to the second group of the **linker** of the **oligonucleotide**-heterofunctional **linker conjugate**, to form the **oligonucleotide-protein conjugate.**

An INDEPENDENT CLAIM is also included for an **oligonucleotide-protein conjugate** produced by (M).

USE - (M) is useful for producing an **oligonucleotide-protein conjugate.** (I) is useful for determining the presence or concentration of a target nucleic acid molecule (preferably a nucleic acid molecule of a pathogen or a tumor cell) in a sample, by contacting the sample with (I), where a sequence of an **oligonucleotide** portion of (I) is selected to be able to hybridize with the target nucleic acid molecule, and detecting a **protein** portion of any of (I) having an **oligonucleotide** portion hybridized to the target nucleic acid molecule, where the detection determines the presence or concentration of the target nucleic acid molecule in the sample. (I) is useful for determining the presence or concentration of a target analyte in a sample, by contacting the sample with (I), where a **protein** portion of (I) is selected to be able to bind to the target analyte, and detecting an **oligonucleotide** portion of any of (I) having a **protein** portion bound to the target analyte, where the detection determines the presence or concentration of the target analyte in the sample (all claimed). (I) is useful for detecting the presence or absence of a nucleic acid sought to be detected in a biological medium, which may contain other nucleic acids that are not sought, or to assay for the presence of binding ligands to the **conjugated protein**, and the presence of concentration of such ligands.

Dwg.0/2

TECH UPTX: 20030630

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M), the **amino group** is at the 3' or 5' end of the **oligonucleotide.** The step of contacting the **oligonucleotide** with the **linker** additionally comprises forming the **oligonucleotide** having the 3' or 5' **amino group.** The **oligonucleotide** having the 3' **amino group** is formed by synthesizing the **oligonucleotide** on a

3'-amino CPG solid support. The **amino group** is at an internal site of the **oligonucleotide.** The step of contacting the **oligonucleotide** with the **linker** additionally comprises forming the **oligonucleotide** having the internal **amino group.** The modified **amino group** is C7 CPG. The first group of the heterofunctional **linker** is an NHS group, and the second group is a maleimide group. The heterofunctional **linker** is selected from sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (**sulfo-SMCC**), N-(epsilon-maleimidocaproyloxy)sulfosuccinimide ester (**sulfo-EMCS**), N-(gamma-maleimidobutyryloxy) sulfosuccinimide ester (**sulfo-GMBS**), N-(K-maleimidoundecanecanoyloxy)sulfosuccinimide ester (**sulfo-KMUS**), m-maleimidobenzoyl-N-hydroxysulfosuccinimide ester (**sulfo-MBS**), sulfosuccinimidyl(4-iodoacetyl)aminobenzoate (**sulfo-SIAB**), sulfosuccinimidyl 4-(p-maleimidophenyl)butyrate (**sulfo-SMPB**), sulfosuccinimidyl-6-(alpha-methyl-alpha-(2-pyridyldithio)toluamido) hexanoate (**sulfo-LC-SMPT**), N-succinimidyl-4-vinylsulfonyl)benzoate (**SVSB**), succinimidyl 6-(4-iodoacetyl)amino methyl-cyclohexane-1-carbonyl)amino hexanoate (**SIACX**), N-succinimidyl iodoacetate or iodoacetic acid N-hydroxysuccinimide ester (**SIA**), succinimidyl 6(6-(((iodoacetyl)amino hexanoyl)aminohexanoate)) (**SIAXX**) and p-nitrophenyl iodoacetate (**NPIA**). The **thiol group** of the **protein** is derived from an iminothiolane moiety. The step of contacting the **oligonucleotide** -heterofunctional **linker conjugate** with a **protein** having a **thiol group**, additionally comprises forming the **protein** having the **thiol group.** The **protein** is formed by reacting the **amino group** of a **protein** with iminothiolane. The **protein** is an enzyme (selected from alkaline phosphatase, beta-galactosidase, horse radish peroxidase and urease), hapten, immunoglobulin (preferably an immunoglobulin that is able to bind to a drug, a receptor, a receptor ligand, a tumor antigen, or an antigen that is characteristic of a pathogen), streptavidin, avidin or phycobillin **protein.**

L35 ANSWER 6 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-713479 [77] WPIDS
DNC C2002-202313
TI New composition, useful as vaccine against bacterial, viral, parasitic or fungal infections, or cancer, in animals and humans, comprises M cell-specific ligand, nucleic acid encoding an immunogen, and a nucleic acid binding moiety.
DC B04 C06 D16
IN PASUAL, D W
PA (RERE-N) RES & DEV INST INC
CYC 100
PI WO 2002072015 A2 20020919 (200277)* EN 102p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2002072015 A2 WO 2002-US7254 20020312
PRAI US 2001-274639P 20010312
AB WO 200272015 A UPAB: 20021129

NOVELTY - A composition comprising an M cell-specific ligand, a nucleic acid sequence encoding an immunogen, and a nucleic acid binding moiety, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine comprising the composition and an excipient;

(2) a method for immunizing a host against an immunogen by administering the vaccine to the host;

(3) a method for assaying for mucosal immunity, comprising:

(a) administering the vaccine to an animal which is free of infection from the infectious agent whose antigen is to be tested;

(b) isolating mucosal immune cells from the animal; and

(c) co-incubating the isolated cells with heterologous antigen expressing or presenting cells, where lysing of antigen expressing cells is indicative of mucosal immunity in the animal;

(4) an isolated nucleic acid encoding a fusion protein comprising a nucleic acid binding moiety and an M cell-specific ligand;

(5) a vector comprising the nucleic acid;

(6) an isolated polypeptide comprising the expression product of the vector, or a nucleic acid binding moiety and an M cell-specific ligand;

(7) a host cell comprising the vector;

(8) a method of expressing a fusion protein, comprising the step of expressing the vector;

(9) an isolated antibody that binds to the polypeptide;

(10) a kit comprising an M cell-specific ligand and a nucleic acid or immunogen binding moiety; and

(11) a pharmaceutical composition formulated for mucosal delivery comprising an M cell-specific ligand and an immunogen.

ACTIVITY - Immunomodulator; Antibacterial; Virucide; Antiparasitic; Antifungal; Cytostatic. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful as a vaccine to induce an immune response against the immunogen or against the disease with which the immunogen is associated (claimed). The kit is useful in delivering a nucleic acid vaccine or other vaccine to mucosal lymphoid tissue, and for measuring a mucosal immune response raised against the nucleic acid vaccine or other vaccine (claimed). The methods are useful for immunizing animals and human subjects against bacterial, viral, parasitic, fungal infectious agents or cancer.

Dwg.0/7

TECH UPTX: 20021129

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: The composition comprises a nucleic acid sequence that is, specifically, a **DNA** sequence. The nucleic acid binding moiety is a **polypeptide** comprising a polymeric chain of basic amino acid residues, such as polylysine. The **polypeptide** is a fusion **protein** further comprising the M cell-specific ligand. The immunogen is selected from immunogens expressed by infectious agents and tumor specific antigens. The infectious agent may be a bacterium, parasite, fungus, virus or a prion, such as tuberculobacillus, leprosy bacillus, malaria parasite, diphtheria bacillus, tetanus bacillus, Leishmania, Salmonella, Schistosoma, measles virus, mumps virus, herpes virus, HIV, cancer or influenza virus. The M cell-specific ligand comprises the **protein** 1 of a reovirus or its tetramer or primer, adhesin derived from Salmonella, adhesin derived from polio virus or M cell tropic fragments. The **DNA** sequence further comprises a plasmid vector in which the **DNA** sequence encoding an immunogen is operably **linked** to transcription tregulatory elements. The above composition further comprises a **linker**, which is a **crosslinker**, and an M cell-specific ligand **conjugated** to an immunogen that is

encapsulated or surface-displayed in a liposome. The **crosslinker**, which is a complexing moiety, consists of SPDP, DSS, **SIAB**, SATA, **MBS** or **GMBS** (undefined). The complexing moiety comprises nitrilotriacetic (NTA)-metal complex and iminodiacetic acid (IDA)-metal. The M cell-specific ligand and the immunogen are **conjugated** or are comprised in a fusion **protein** or **polypeptide.**

Preferred Vaccine: The vaccine, which is a therapeutic vaccine, induces a protective immune response in a vaccinated host against the immunogen. The vaccine further comprises an adjuvant consisting of an immunomodulator. The immunomodulator comprises cytokines, lymphokines, interleukins, interferons or growth factors. The vaccine, which is formulated in unit dosage form, is further packaged with instructions for use.

Preferred Method: In assaying for mucosal immunity, the mucosal immune cells are isolated from tissues selected from lamina propria tissue, intraepithelial tissue, Peyer's patches, lymph nodes, nasal passages, NALT, adenoids, and vaginal epithelium. This method further comprises the step of evaluating the animal's cytokine profile.

Preferred Vector: The vector, which is an expression vector, comprises a nucleic acid that is in operable **linkage** consisting of sense and antisense orientations relative to transcriptional elements comprising the vector.

Preferred Kit: The kit further comprises instructions for its use.

L35 ANSWER 7 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-373742 [41] WPIDS
DNC C2002-105869
TI A single chain insulin analog (**SIA**) compound used in the treatment of type I diabetes, comprises the properties of greater insulin receptor binding activity than proinsulin and less insulin receptor binding activity than insulin.
DC B04 D16
IN KIM, K; KIM, S; LEE, H C; SHIN, H; YOON, J; KIM, G S; KIM, S J; SHIN, H C; KIM, K S
PA (LEEH-I) LEE H C; (KIMK-I) KIM K S; (KIMS-I) KIM S; (SHIN-I) SHIN H; (YOON-I) YOON J
CYC 29
PI EP 1193272 A1 20020403 (200241)* EN 24p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
KR 2002026756 A 20020412 (200267)
JP 2002320490 A 20021105 (200304) 19p
US 6630348 B1 20031007 (200374)
ADT EP 1193272 A1 EP 2001-121651 20010913; KR 2002026756 A KR 2000-58003 20001002; JP 2002320490 A JP 2001-306269 20011002; US 6630348 B1 US 2000-706690 20001107
PRAI US 2000-706690 20001107; KR 2000-58003 20001002
AB EP 1193272 A UPAB: 20020701
NOVELTY - A single-chain insulin analog (**SIA**) compound (I) comprising the properties of greater insulin receptor binding activity than proinsulin and less insulin receptor binding activity than insulin, is new.

DETAILED DESCRIPTION - A single-chain insulin analog compound (I) comprises the properties of greater insulin receptor binding activity than proinsulin and less insulin receptor binding activity than insulin. (I) has the formula:

B chain - X - A chain (I);

B and A = human insulin chains or functional analogs; and

X = a joining peptide of 5 to 18 amino acids.

INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide encoding (I);
(2) a recombinant vector comprising the polynucleotide;
(3) a cell line transformed with the vector;
(4) treating (M1) a patient suffering from diabetes comprises:
(a) generating a recombinant viral or plasmid vector comprising a polynucleotide encoding a single-chain insulin analog operatively **linked** to a promoter; and
(b) introducing the recombinant viral or plasmid vector to patient, so that expression of polynucleotide results in remission of diabetes;
(5) treating (M2) a patient suffering from diabetes comprises administering (I) to a patient.
ACTIVITY - Antidiabetic.
rAAV-LPK-**SIA** (recombinant adeno-associated virus-L-type pyruvate kinase gene promoter-single-chain insulin analog) was administered into diabetic NOD mice by intraportal injection and monitored the blood glucose levels. The blood glucose levels gradually decreased in the rAAV-LPK-**SIA**-treated NOD mice (10 virus particles), reached the level of normoglycemia at 7 days after treatment, and remained in a normoglycemic state for more than 5 months. In contrast, diabetic NOD mice treated with rAAV-**SIA** (without the LPK promoter) remained hyperglycemic and died within 3 weeks. When the presence of the **SIA** gene in the hepatocytes of NOD mice were examined at 15 weeks after treatment with rAAV-LPK-**SIA**, it was discovered that **SIA DNA** was integrated into the chromosomal **DNA** . **SIA** expression was then examined in the liver and plasma of the mice after glucose loading at 5, 10, and 15 weeks after treatment with rAAV-LPK-**SIA**, and found that **SIA** mRNA was clearly expressed and **SIA** protein was released in the plasma. Anti-**SIA** antibody was not detected in the sera from these mice during the 5 months after treatment.
MECHANISM OF ACTION - Single-chain insulin analog (claimed); Gene therapy.
USE - (I) is used to treat type I diabetes mellitus (claimed).
Dwg.0/4

TECH UPTX: 20020701
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: X is preferably 6-9 amino acids and has the formula:
U1-Zn-Ym-Z1-Un;
U = arginine or lysine residue;
Z = amino acid residue;
Y = a peptide;
1 = an integer of 2-n;
n = an integer of 0, 1 or 2; and
m = an integer of 2 to 5.
Preferably, Z is glycine and Y is gly-pro-gly, ala-pro-gly-asp-val, tyr-pro-gly-asp-val or his-pro-gly-asp-val.
Preferred Vector: The vector may be a plasmid or a virus such as an adeno-associated virus. Preferably the vector comprises an inducible promoter, regulated by glucose, such as pyruvate kinase gene promoter, or preferably, a hepatocyte-specific L-type pyruvate kinase gene promoter.
Preferred Method: The viral vector in (M1) is an adeno-associated virus comprising an inducible promoter, regulated by glucose. In the treatment of diabetes, the diabetes is type I diabetes and the vector is introduced to the patient through the cell line which is transformed with the vector.
Preparation: (I) is prepared by standard genetic recombinant techniques.

L35 ANSWER 8 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-268789 [31] WPIDS
DNC C2002-079652
TI Gene-delivery compound for targeted gene delivery, comprises single-chain

binding polypeptide having effector segment with cysteinyl residue and nucleic acid-binding/lipid-associating moiety coupled to polypeptide by residue.

DC A96 B04 D16

IN HUSTON, J S; LAURENT, O; MARASCO, W A; SCHERMAN, D; WILS, P; ZHU, Q; QUAN, Z

PA (HUST-I) HUSTON J S; (LAUR-I) LAURENT O; (MARA-I) MARASCO W A; (SCHE-I) SCHERMAN D; (WILS-I) WILS P; (ZHUQ-I) ZHU Q; (QUAN-I) QUAN Z

CYC 96

PI WO 2002000914 A2 20020103 (200231)* EN 96p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001070142 A 20020108 (200235)
US 2002132990 A1 20020919 (200264)

ADT WO 2002000914 A2 WO 2001-US20182 20010625; AU 2001070142 A AU 2001-70142 20010625; US 2002132990 A1 Provisional US 2000-213653P 20000623, US 2001-888721 20010625

FDT AU 2001070142 A Based on WO 2002000914

PRAI US 2000-213653P 20000623; US 2001-888721 20010625

AB WO 200200914 A UPAB: 20021031
NOVELTY - A gene-delivery compound (I) comprising a single-chain binding polypeptide (SCBP) having at least one effector segment having a cysteinyl residue and a nucleic acid-binding moiety (NABM) or a lipid-associating moiety (LAM) coupled to SCBP by the residue, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition (II) comprising (I) and a nucleic acid associated reversibly with NABM, or a liposome in association with LAM.
ACTIVITY - None given in the source material.
MECHANISM OF ACTION - Gene therapy. No supporting data is given.
USE - (I) is useful for targeted gene delivery for treating diseases by gene therapy.
ADVANTAGE - (I) is utilized to provide targeted non-viral delivery of gene to target cells, and (I) having the ability to bind to multiple, different surface markers on a target cell, can be utilized for multi-site targeting.
Dwg.0/26

TECH UPTX: 20020516
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: In (I), the binding region of SCBP is effective in binding two or more surface markers of a mammalian cell, and comprises a single-chain Fv protein, where the marker is a tumor antigen from erbB-2, erbB-3, erbB-4, p53, p21 ras, transferrin receptor, Lewis Y antigen, carcinoembryonic antigen, epidermal growth factor, MUC1, and any other tumor-associated or tumor-specific antigen. NABM is preferably from salmon protamine, subfragments of salmon protamine, human histone H1, subfragments of human histone H1, human protamine, subfragments of human protamine, HMG, polylysine or any other **DNA** binding polypeptide; and LAM is from linear, branched, cyclic, and polycyclic compounds capable of insertion into and retention of lipid-containing compositions, where LAM contains polyethylene glycol (PEG) and preferably is maleimide-PEG-(C18)2, in which the PEG portion has about 10-100 oxyethyl units. (I) further comprises an additional effector segment that binds reversibly with nucleic acids, or that facilitates endosomal escape or avoidance, non-endosomal transport in a cell, or entry into the nucleus of a targeted cell, where the effector segment is a human histone H1 peptide sequence which comprises the carboxyl-terminal sequence that binds to the KDEL receptor in the Golgi, SEKDEL, or comprises SV40

large T antigen nuclear localization sequence, TPPKKKRKV. (I) further comprises a spacer sequence which is located between the effector segment containing the cysteinyl residue and an additional effector segment, where the spacer sequence comprises one or two segments of SSSSG or GGGGS. In (I), the cysteinyl residue is coupled to NABM by a heterobifunctional **crosslinking** agent which is preferably from succinimidyl trans-4(maleimidylmethyl)-cyclohexane-1-carboxylate (**SMCC**) and sulfoSMCC.

Preferred Composition: In (II), the nucleic acid comprises **DNA** encoding a therapeutic gene which is a lymphokine, a tumor necrosis factor, or an intrabody; or is from tumor suppressor genes, p53, proapoptotic genes, suicide genes, prodrug converting genes, HSV-TK and anti-angiogenic genes. In (II) comprising a liposome, SCBP is located on a surface of the liposome which is a stealth liposome.

L35 ANSWER 9 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-216898 [27] WPIDS
DNC C2002-066275
TI New integrase inhibiting compounds useful for development of anti-viral therapeutics comprises a **linker** group, a functional group bonded to **linker** group, and a bond between functional and **linker** groups.
DC B04 B05 D16
IN HARRISON, R W; SKALKA, A M
PA (UYJE-N) UNIV JEFFERSON THOMAS
CYC 21
PI WO 2002002516 A2 20020110 (200227)* EN 42p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CA JP
ADT WO 2002002516 A2 WO 2001-US19923 20010622
PRAI US 2000-215474P 20000630
AB WO 200202516 A UPAB: 20020429
NOVELTY - An integrase inhibiting compound (I) comprises a **linker** group (a), a functional group (b) bonded to (a) and a bond (c) between (b) and (a). (a) comprises a rigid aromatic or nonaromatic compound, (b) comprises at least one derivatized mono or polycyclic aromatic group (preferably aromatic phenylnaphthyl group) and (c) comprises a flexible **linkage.**

DETAILED DESCRIPTION - An integrase inhibiting compound (I) comprises a **linker** group (a), a functional group (b) bonded to (a) and a bond (c) between (b) and (a). (a) comprises a rigid aromatic or nonaromatic compound with at least one (b) replacing an atom of the rigid aromatic or non-aromatic compound. (b) comprises at least one derivatized mono or polycyclic aromatic group (preferably aromatic phenylnaphthyl group) and (c) comprises a flexible **linkage.**

An INDEPENDENT CLAIM is included for inhibiting an integrase involving binding (I) to an integrase, inhibiting a catalytic activity of the integrase and then inhibiting an essential function in viral replication of the retrovirus.

ACTIVITY - Anti HIV.

MECHANISM OF ACTION - HIV (human immuno deficiency virus) and ASLV (avian sarcoma-leukosis virus) integrase inhibitors. Hela cells (5 multiply 104) were plated and were analyzed for each concentration. On the following day, a HIV-based retroviral vector containing lacz receptor gene described in Naldinin et al. Science, 272: 263 - 267, 1996 was added to each well for 2 hours in the presence of RWH35 (7-amino, 4-hydroxy, 2-naphthalene sulfonic acid and 1 equivalent of alpha , alpha '-dibromomethyl meta-xylene dissolved in DMSO (i.e. inhibitor compound)) and dextran (5 mg/ml). After 2 hours, the HIV vector was removed and fresh medium containing the inhibitor was added. Inhibitor was kept on cells for

another 16 hours, then removed and fresh medium added. Cells were stained 2 days post infection using a beta -gal assay performed according to the transfection **MBS** (mammalian transfection kit) (stratagene). The compound had an IC50 value of 0.7 micro M for HIV integrase.

USE - For inhibiting integrase and for further development of a therapeutic agent that causes inhibition of the integrase (claimed) essential in the life cycle of retroviruses.

ADVANTAGE - The compound inhibits the integrase, essential in the life cycle of retroviruses; allows the examination of the HIV integrase binding site and subsequently the mechanism of inhibition of enzyme activity. The compound has a restricted conformation for the determination of the integrase binding site and mechanism of inhibition and is effective in the submicromolar range and provides new lead compounds for the development of anti-viral therapeutics. The compound inhibits catalytic activity of the integrase thus inhibiting an essential function in viral replication of the retrovirus.

Dwg.0/7

TECH UPTX: 20020429

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Functional Group: (b) further comprises mimicking nucleotides or bases of a **DNA** comprising placement into a stable hydrogen bonding and base stacking geometry on the integrase.

Preferred Method: (I) binds at or close to the active site on the integrase binds in a site distal or distinct from the **DNA** binding site on the integrase binds directly to a viral **DNA** -integrase complex or to a viral and host **DNA**-integrase complex. (I) inhibits the integrase by inhibiting a viral integration, a viral **DNA** into a host **DNA.** The method further involves an inhibition of a processing step of the integration of the viral **DNA** into the host **DNA.** The inhibition of the integrase further involves inhibition of replication of a virus at concentrations below cell toxicity.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: (I) comprises a symmetric or an asymmetric compound. The compound comprises a mixture of 8-bromo, 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid; diaminomethyl meta-xylene **linker** group with two functional groups comprising 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid (preferably 8-bromo, 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid).

Preferred Components: (b) is selected from para-aminobenzamidine; para-amino benzoic acid; 2,6-diaminoanthraquinone; 5-amino, 8-hydroxy quinoline; and 7-amino, 4-hydroxy, 2-naphthalene sulfonic acid. (a) is selected from meta-xylene, para-xylene, 2,6-dimethylpyridine or 1,4-diamino-2,3-butanediol. The rigid aromatic compound is a planar rigid aromatic compound.

L35 ANSWER 10 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-106127 [14] WPIDS
DNC C2002-032542
TI Novel vector comprising double stranded DNA having target sequence and chimeric molecule comprising sequence specific polyamide moiety bound non-covalently to target and ligand moiety covalently **linked** to polyamide.
DC B04 D16
IN BIANCHI, E; FATTORI, D; INGALLINELLA, P; KINZEL, O; PESSI, A
PA (RICE-N) IST RICERCHE BIOL MOLECOLARE ANGELETTI; (BIAN-I) BIANCHI E; (FATT-I) FATTORI D; (INGA-I) INGALLINELLA P; (KINZ-I) KINZEL O; (PESS-I) PESSI A
CYC 24
PI WO 2001088160 A2 20011122 (200214)* EN 98p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

W: AU CA JP US
AU 2001058708 A 20011126 (200222)
EP 1290198 A2 20030312 (200320) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
US 2003207400 A1 20031106 (200374)
ADT WO 2001088160 A2 WO 2001-IB980 20010511; AU 2001058708 A AU 2001-58708 20010511; EP 1290198 A2 EP 2001-932034 20010511, WO 2001-IB980 20010511; US 2003207400 A1 WO 2001-IB980 20010511, US 2003-276734 20030512
FDT AU 2001058708 A Based on WO 2001088160; EP 1290198 A2 Based on WO 2001088160
PRAI GB 2000-11938 20000517
AB WO 200188160 A UPAB: 20020301
NOVELTY - A vector (conjugate) (I) comprising a double-stranded DNA (dsDNA) (Ia) having at least one target sequence (T); and a chimeric molecule (Ib) which comprises (i) a sequence specific polyamide (SSP) moiety bound non-covalently to (T); and (ii) a ligand moiety (L) covalently **linked** to SSP, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising (I) and a carrier;

(2) synthesis (M1) of SSP on a solid support involving:

(a) attaching an N-terminal of the polyamide to the solid support via a safety-catch **linker**, -S(=O)2-NH-; and

(b) following synthesis of the polyamide, removing it from the solid support by cleavage of the safety-catch **linker** by activation and nucleophilic attachment;

(3) introducing (M2) a dsDNA into a cell or a sub-cellular compartment involving:

(a) providing (Ib) which comprises SSP and (L) **linked** covalently to the SSP moiety, and capable of being directed to the cell or the sub-cellular compartment;

(b) providing a dsDNA which includes a target sequence for the SSP moiety, under conditions where (Ib) binds to the dsDNA to provide a vector; and

(c) bringing the vector into contact with the cell under conditions for uptake of the vector and transport of the dsDNA;

(4) a eukaryotic cell obtained by (M2); and

(5) progeny of a eukaryotic cell obtained by (M2).

ACTIVITY - Antibacterial; Virucide.

MECHANISM OF ACTION - Gene therapy; Vaccine.

No biological data given.

USE - (I) Is useful in a method of treatment of the human or animal body and for preparing a medicament for treating a condition treatable by gene therapy. (I) Is also useful in gene therapy techniques. (M2) is useful for introducing a dsDNA into the nucleus of a eukaryotic cell which involves providing (Ib) which comprises SSP and (L) **linked** covalently to SSP moiety and capable of being directed to the nucleus of the eukaryotic cell; providing a dsDNA which includes a target sequence for the SSP moiety, under conditions where (Ib) binds to the dsDNA provide a vector; and bringing the vector into contact with the eukaryotic cell under conditions for uptake of the vector and transport of the dsDNA. The vector is brought into contact with the eukaryotic cell in vivo, ex vivo or in vitro. The eukaryotic cell is preferably a CHO cell (all claimed). (I) is also used to deliver **DNA** encoding antigens (viral antigens, bacterial antigens or host **protein** antigens) useful as vaccines.

Dwg.0/4

TECH UPTX: 20020301
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) Is synthesized by the process which includes the step of synthesis of SSP by (M1).

Preferred Vector: (I) Further comprises one or more sequences designed to facilitate homologous recombination to a specific locus within a host cell. (I) Comprises two or more (Ib) which comprise different ligand moieties. (Ia) has more than one (T) (in the range of 2-100, and preferably 6-10 target sequences), which is not present in the promoter or coding sequence part of the vector. (T) is at least 6 bases in length, preferably 10-20 bases in length. (Ia) Is linear, circular or a circular supercoiled **DNA.** (Ia) Further comprises dsDNA sequences of human, non-human animal, vegetable, bacterial or viral origin, and also comprises one or more transcribable sequences from promoters, and origins of replication, one or more selectable or detectable markers. (Ia) Comprises a transcribable **DNA** sequence which, when transcribed from the **DNA** under the control of a promoter (a) brings about an therapeutic effect, (b) yields mRNA for the expression of a **protein**, or (c) yields RNA which itself has a function as an anti-sense RNA or a ribozyme. (Ia) Comprises one or more coding sequences designed to modify tumor cells so that the tumor cells may be destroyed or inactivated. (Ia) Further comprises (a) one or more genes encoding enzymes capable of activating pro-drugs into active toxic drugs, (b) one or more tumor suppressor genes, (c) genes encoding cytokines or cell surface markers of immunoglobulin superfamily, (d) one or more functional copies of a gene, (e) **DNA** antigens useful as vaccines, or (f) one or more consecutive promoters and tissue specific promoters. SSP comprises at least 6 organic heterocyclic groups at least some of which are pyrrole and imidazole groups, preferably at least 7 organic heterocyclic groups (e.g. optionally substituted pyrrole, imidazole, pyrazole, triazole, furan, thiophene, oxazole, thiazole, or cyclopentadiene) or comprises 8-30 (preferably 18) organic cyclic groups. At least 60% (preferably 100%) of the organic cyclic groups or the organic heterocyclic groups which have 5 or 6 (preferably 5) annular members. The organic heterocyclic groups have 1-3 annular heteroatoms such as nitrogen, oxygen or **sulfur.** The organic heterocyclic **groups** have 1-2 annular nitrogen heteroatoms, and are preferably optionally substituted pyridine, pyrimidine, or triazine, where one or more annular NH groups are substituted with 1-3C alkyl groups (preferably Me). SSP comprises the organic heterocyclic groups (N-methyl pyrrole (Py) or N-methyl imidazole) having 5 annular members, and 1-2 annular nitrogen atoms of which one is methylated. The SSP further comprises one or more (2-6, preferably 4) optionally substituted aliphatic **amino** acid **groups** (e.g. glycine, beta alanine or gamma amino butyric acid) having a chain of 2-6 carbon atoms. The SSP comprises the optionally substituted **amino** acid **group** having a chain of 2-6 carbon atoms, proximal to one terminus of the moiety. (I) Comprises no consecutive sequence of 6 heterocycles, and where the organic cyclic **groups** and aliphatic **amino** acid **groups**, if present, are joined by **linking** groups having a length of 2 atoms where at least some of the **linking** groups will have NH groups. The **linking** groups are preferably methyleneamino (-CH2-NH-), carboxamide (-C(=O)NH-), ethylene (-CH2CH2-), thiocarboxyamide (-C(=S)NH-), or carboxyamidinoyl (-C(=NH)NH-). Preferably, the **linking** groups are carboxamide (preferred), thiocarboxamide, or carboxamidinoyl. One or both of termini of SSP has a polar **group** (e.g. **amino**, hydroxyl, or mercapto) substituted on an alkyl group, where the polar group is from 2-6 carbon atoms from the **linkage** to the remaining molecule. At pH less than 8, the **amino group** is positively charged. Alternately, the polar group may also be optionally substituted aminopropyl or N-methylaminopropyl, where the SSP has one or two complementary pairs, each of which includes a N-methyl imidazole group and specificity of one nucleotide. (L) is capable of directing the **conjugate** to a

cellular or subcellular location, preferably to the nucleus of a eukaryotic cell, in which case the ligand moiety is a general nuclear localization signal. (L) (a) is a **protein** or **polypeptide** capable of binding a target receptor, (b) is a **protein** or **polypeptide** based on hormones or other signaling **proteins** which bind to a target on the surface of a cell, or (c) comprises a hybrid **protein** which includes a component to direct the **conjugate** to a particular target cell, and a component to promote uptake of the **conjugate** by the cell. (L) is insulin, asialoglycoprotein or its synthetic analogues, transferrin, malaria circumporozoite **protein** , RGD analogues or endoosmolitic **peptide.** The ligand moiety is a growth factor which binds to a receptor, or is an antibody or its fragment. (L) is a carbohydrate or mannose.
Preferred Method: In (M1), the safety catch **linker** comprises a **linkage** -C(=O)-CH2CH2CH2-S(=O)2-NH-, -C(=O)-CH2CH2CH2-S(=O)2-NH-C(=O)-. The activation is achieved by reaction with iodoacetonitrile. The nucleophilic attack is achieved by reaction with amine or thiol. The polyamide is synthesized using one or more of the reagents (R1), (R2) or (R3) as given in the specification.

L35 ANSWER 11 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-308249 [32] WPIDS
CR 1997-558673 [51]
DNC C2001-095229
TI New lipid vesicle having a bilayer membrane that has a positive net charge at physiological pH for use in cosmetic, pharmaceutical or diagnostic applications.
DC B04 B07
IN GLUECK, R; KLEIN, P; WALTI, E R; WAELTI, E R
PA (NIKA-N) NIKA HEALTH PROD LTD
CYC 94
PI WO 2001026628 A1 20010419 (200132)* EN 44p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000077850 A 20010423 (200147)
NO 2002001607 A 20020607 (200250)
EP 1217990 A1 20020703 (200251) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
SK 2002000478 A3 20020910 (200274)
CZ 2002001216 A3 20021016 (200279)
HU 2002002809 A2 20021228 (200308)
KR 2002063872 A 20020805 (200308)
JP 2003512306 W 20030402 (200325) 43p
EP 1217990 B1 20040128 (200410) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2001026628 A1 WO 2000-EP9540 20000929; AU 2000077850 A AU 2000-77850 20000929; NO 2002001607 A WO 2000-EP9540 20000929, NO 2002-1607 20020405; EP 1217990 A1 EP 2000-967824 20000929, WO 2000-EP9540 20000929; SK 2002000478 A3 WO 2000-EP9540 20000929, SK 2002-478 20000929; CZ 2002001216 A3 WO 2000-EP9540 20000929, CZ 2002-1216 20000929; HU 2002002809 A2 WO 2000-EP9540 20000929, HU 2002-2809 20000929; KR 2002063872 A KR 2002-704325 20020404; JP 2003512306 W WO 2000-EP9540 20000929, JP 2001-529418 20000929; EP 1217990 B1 EP 2000-967824 20000929, WO 2000-EP9540 20000929
FDT AU 2000077850 A Based on WO 2001026628; EP 1217990 A1 Based on WO

2001026628; SK 2002000478 A3 Based on WO 2001026628; CZ 2002001216 A3 Based on WO 2001026628; HU 2002002809 A2 Based on WO 2001026628; JP 2003512306 W Based on WO 2001026628; EP 1217990 B1 Based on WO 2001026628

PRAI US 1999-414872 19991008

AB WO 200126628 A UPAB: 20040210

NOVELTY - A lipid vesicle having a bilayer membrane that has a positive net charge at physiological pH. The vesicle further comprises at least one active fusogenic peptide and optionally phosphatidyliethanolamine (PE) and/or cationic lipids other than 1,3-dioleoyloxy-2-(6-carboxy-spermyl)-propylamide (DOSPER).

DETAILED DESCRIPTION - A lipid vesicle having a bilayer membrane that has a positive net charge at physiological pH, the vesicle further comprises at least one active fusogenic peptide that is a non-Sendai viral hemagglutinin that causes the vesicles to be internalized by target cells through receptor-mediated phagocytosis or endocytosis, characterized in that the vesicle membrane comprises 5-30% by weight, based on total membrane lipids of DOSPER and a balance of 95-70% by weight of other lipids comprising phosphatidylcholine (PC) or a derivative and optionally phosphatidyliethanolamine (PE) and/or cationic lipids other than DOSPER.

INDEPENDENT CLAIMS are also included for:

(1) a process for the manufacture of a lipid vesicle, which comprises;

(1) preparing a buffer solution that comprises a non-ionic detergent and that further comprises DOSPER and other lipids and at least one active fusogenic peptide that is a non-Sendai viral hemagglutinin that causes the vesicles to be internalized by target cells through receptor-mediated phagocytosis or endocytosis;

(2) adjusting the lipid concentration to 5-30% by weight of DOSPER and to a balance of 95-70% by weight of other lipids comprising PC or a derivative and optionally PE and/or cationic lipids other than DOSPER; and

(3) removing the detergent by dialysis or by treating the solution with microcarrier beads, resulting in the formation of positively charged lipid bilayer vesicles; and

(2) use of a vesicle for the manufacture of a composition for cosmetic, diagnostic or medical applications, particularly for delivering a desired drug or substance to resting or proliferating target cells.

USE - A composition comprising more than one vesicle can be used in cosmetic, pharmaceutical or diagnostic applications (claimed). The target cells are selected from the group consisting of cancer cells, leukemic cells and virally infected cells.

ADVANTAGE - When using DOSPER as a cationic lipid in combination with other lipids, high performance virosomes can be produced that even exceed up to ten times the already high transfection efficiency of the N-((1,2,3-dioleoyloxy)-propyl)-N,N,N-trimethylammoniummethyl-sulfate (DOTAP) virosomes of WO97/41834.

Dwg.0/13

TECH UPTX: 20010611

TECHNOLOGY FOCUS - BIOLOGY - Preferred components: The vesicle further contains a desired drug or substance (I) for delivery to target cells, which is preferably negatively charged and particularly selected from a group consisting of a dye, a tracer substance, a cosmetic agent, and a nucleic acid material, selected from a group consisting of short chain **DNA** or RNA, deoxyribonucleotides, oligodeoxyribonucleotides, oligodeoxyribonucleotide selenoates, oligodeoxyribonucleotide phosphorothioates, oligodeoxyribonucleotide phosphoramidates, oligodeoxyribonucleotide methylphosphonates, **peptide** nucleic acids, ribonucleothioates, oligoribonucleotides, oligoribonucleotide phosphorothioates, 2'-Ome-oligoribonucleotide phosphates, 2'-Ome-oligoribonucleotide phosphorothioates, ribozymes, genes, plasmids and vectors.

The nucleic acid material preferably comprises at least one antisense **oligonucleotide**, preferably an antisense **oligonucleotide** that is targeting protooncogene or oncogene encoded mRNA.
The vesicle further comprises at least one cell-specific marker attached to the vesicle membrane, which further comprises PE and a bifunctional **crosslinker** which is **linked** with one of its binding sites to a free **amino group** of the PE and with its other binding site to the cell specific marker. The cell-specific marker is a **protein** for binding to a receptor of target cells selected from the group consisting of an antibody, an antibody fragment, a cytokine and a growth factor.
The hemagglutinin is derived from a virus selected from the group consisting of rhabdovirus, parainfluenza virus type III, Semliki Forest virus and togavirus.
The non-ionic detergent is octaethyleneglycol monododexylether (C12E8) or n-octyl-oligooxyethylene.
The **crosslinking** agent is a heterobifunctional organic molecule having at least one maleimido and at least one carboxyl group, and is preferably selected from the group consisting of bis-N-succinimidyl derivatives and photactivatable succinimidyl derivatives.
Preferred compositions: The vesicle comprises the nucleic acid material in an amount 0.03-0.1, preferably 0.045-0.065 microg per 1 microg DOSPER. The average vesicle diameter is 120-180 nm. The vesicle membrane comprises DOSPER in a concentration of 10-30%, preferably 20-25% by weight, based on total membrane lipids. The vesicle membrane comprises 25% by weight of DOSPER and 75% by weight of PC, preferably dioleoylphosphatidylcholine (DOPC).
Preparation: The process for the manufacture of the lipid vesicle further comprises:
(a) incorporating a quantity of (I) for delivery to target cells into the vesicles; and
(b) preparing **conjugate** molecule complexes consisting of phosphatidylethanolamine (PE), a bifunctional **crosslinker**, and a cell-specific marker in a way such that the bifunctional **crosslinker** with one binding site **links** to the **amino group** of PE and with another one to a **thiol group** of the cell-specific marker, removing unconjugated material and adding molecule complexes to the solution of step (1).
Incorporation of (I) is accomplished by adding it to the solution in step (1) and in step (3) vesicles containing (I) are formed. Incorporation of (I) into the vesicles is preferably accomplished by adding to the vesicles from (3), sonicating the mixture to integrate (I) into the vesicles and removing non-integrated material, preferably by gel filtration.
Positively charged lipid complexes or liposomes, comprising 50-100% by weight, based on their total lipid contents, of DOSPER lipid, with (I) can be added to the vesicles.
The manufacture of the composition, comprises incubating target cells in vitro in the presence of the vesicle and optionally transferring the incubated target cells to an organism in vivo. Metabolic or proliferative activity of the target cells is reduced upon incubation in the presence of the vesicle.

L35 ANSWER 12 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-273770 [28] WPIDS
DNN N2001-195557 DNC C2001-083075
TI New modified peptide nucleic acids and **oligonucleotides**, useful for treating and preventing bacterial infections and disinfecting non-living objects.
DC B04 D16 D22 P34

IN BECK, F; GIWERCMAN, B K; GOOD, L; HANSEN, H F; MALIK, L; NIELSEN, P E; SCHOU, C; WISSENBACH, M

PA (PANT-N) PANTHECO AS; (NIEL-I) NIELSEN P E; (BECK-I) BECK F; (GIWE-I) GIWERCMAN B K; (GOOD-I) GOOD L; (HANS-I) HANSEN H F; (MALI-I) MALIK L; (SCHO-I) SCHOU C; (WISS-I) WISSENBACH M

CYC 95

PI WO 2001027261 A2 20010419 (200128)* EN 73p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000077730 A 20010423 (200147)
NO 2002001711 A 20020611 (200252)
EP 1220902 A2 20020710 (200253) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 2000014756 A 20020709 (200254)
HU 2002003465 A2 20030128 (200323)
CN 1387567 A 20021225 (200324)
US 6548651 B1 20030415 (200329)
JP 2003511466 W 20030325 (200330) 99p
US 2003176325 A1 20030918 (200362)
ZA 2002002455 A 20030827 (200362) 109p
US 2003199431 A1 20031023 (200370)

ADT WO 2001027261 A2 WO 2000-DK580 20001013; AU 2000077730 A AU 2000-77730 20001013; NO 2002001711 A WO 2000-DK580 20001013, NO 2002-1711 20020411; EP 1220902 A2 EP 2000-967618 20001013, WO 2000-DK580 20001013; BR 2000014756 A BR 2000-14756 20001013, WO 2000-DK580 20001013; HU 2002003465 A2 WO 2000-DK580 20001013, HU 2002-3465 20001013; CN 1387567 A CN 2000-815281 20001013; US 6548651 B1 Provisional US 1999-159679P 19991015, Provisional US 1999-159684P 19991015, Provisional US 2000-211435P 20000614, Provisional US 2000-211758P 20000614, Provisional US 2000-211878P 20000614, US 2000-689155 20001012; JP 2003511466 W WO 2000-DK580 20001013, JP 2001-530466 20001013; US 2003176325 A1 Provisional US 1999-159679P 19991015, Provisional US 1999-159684P 19991015, Provisional US 2000-211435P 20000614, Provisional US 2000-211758P 20000614, Provisional US 2000-211878P 20000614, Div ex US 2000-689155 20001012, US 2001-83259 20011019; ZA 2002002455 A ZA 2002-2455 20020327; US 2003199431 A1 Provisional US 1999-159679P 19991015, Provisional US 1999-159684P 19991015, Provisional US 2000-211435P 20000614, Provisional US 2000-211758P 20000614, Provisional US 2000-211878P 20000614, Div ex US 2000-689155 20001012, US 2002-109274 20020327

FDT AU 2000077730 A Based on WO 2001027261; EP 1220902 A2 Based on WO 2001027261; BR 2000014756 A Based on WO 2001027261; HU 2002003465 A2 Based on WO 2001027261; JP 2003511466 W Based on WO 2001027261; US 2003199431 A1 Div ex US 6548651

PRAI US 2000-211878P 20000614; DK 1999-1467 19991013; DK 1999-1471 19991013; US 1999-159679P 19991015; US 1999-159684P 19991015; DK 1999-1734 19991203; DK 1999-1735 19991203; DK 2000-522 20000328; DK 2000-670 20000419; DK 2000-671 20000419; US 2000-211435P 20000614; US 2000-211758P 20000614

AB WO 200127261 A UPAB: 20010522
NOVELTY - A modified peptide nucleic acid (PNA), is new.
DETAILED DESCRIPTION - A modified peptide nucleic acid (PNA) (I) of formula (F1), is new.
Peptide-L-PNA (F1), where
L = **linker** or a bond;
Peptide = any amino acid sequence; and

PNA = Peptide nucleic acid and a pharmaceutically acceptable salt.
INDEPENDENT CLAIMS are also included for the following:
(1) a modified peptide nucleic acid (PNA) of formula (F1);
(2) a modified **oligonucleotide** (II) of formula Peptide-L-Oligon (F2);
(3) a modified PNA molecule (III) comprising one of 120 fully defined sequences as given in the specification such as H-KFFKFFKFFK-ado-CAT AGC TGT TTC-NH2, H-FFKFFKFFK-ado-CAT AGC TGT TTC-NH2 and H-FKFFKFFK-ado-CAT AGC TGT TTC-NH2;
(4) use of (I)-(III) (in the manufacture of a medicament) for the treatment of infectious diseases, such as bacterial infections;
(5) treating an infectious disease comprising administering to a patient (I), (II) or (III);
(6) disinfecting (M1) non-living objects comprising administering one or more (I), (II) or (III);
(7) use of (I) or (III) in the identification of PNA sequences which are effective in blocking essential functions in bacteria, where different PNA sequences are incorporated in the modified PNA molecule and tested for their ability to inhibit or reduce bacterial growth; and
(8) identifying a PNA sequence, which is useful in inhibiting or reducing bacterial growth comprising mixing (I) or (III) containing different PNA sequences with bacteria, where the selected PNA sequences are complementary to nucleotide sequences for the bacteria and identifying the PNA sequences which are effective in inhibiting or reducing bacterial growth.
ACTIVITY - Antibacterial.
(I) and (III) were tested for antibacterial effect in vivo according to the test described by N. Frimodt-Moller. Untreated animals developed fulminant clinical signs of infection. At all time points (I) and (III) suppressed the Escherichia coli cell forming units/ml compared to non-treated controls and was as efficient as the 2 positive controls.
MECHANISM OF ACTION - Antisense therapy.
USE - (I)-(III) are useful for disinfecting non-living objects and for treating or preventing infectious diseases (claimed), particularly those caused by microorganisms resistant to antibiotics, such as methicillin-resistant and methicillin-vancomycin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus faecalis and Enterococcus faecium, penicillin-resistant Streptococcus pneumoniae and cephalosporin and quinolone resistant gram negative rods e.g. Escherichia coli, Klebsiella pneumoniae, Pseudomonas and Enterobacter species.
ADVANTAGE - PNA polyamide backbones are not recognized by nucleases or proteases and as a result are resistant to degradation by enzymes unlike nucleic acids and peptides.
Dwg.0/7

TECH UPTX: 20010522
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compound: The **linking** group in (III) is -achc-beta.ala-, -achc-ado-, -lcsmcc-beta.ala-, -**mbs**-beta.ala-, -**emcs**-beta.ala-, -Icsmcc-ado-, -**mbs**-ado-, -**emcs**-ado- or -smph-ado-. Preferably the peptide is (KFF)3K and subunits comprising at least 3 amino acids, particularly (KFF)3.
Preferred Method: M1 is useful for disinfecting surgery tools, hospital inventory, dental tools, slaughterhouse inventory and tools or dairy inventory and tools.

L35 ANSWER 13 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-138654 [14] WPIDS
CR 2002-188688 [24]
DNC C2001-041027
TI New isolated polynucleotide useful for outer membrane vesicle preparation

from Gram-negative bacterial strain for vaccination of microbial infections.

DC B04 D16

IN BERTHET, F J; DALEMANS, W L J; DENOEL, P; DEQUESNE, G; FERON, C; LOBET, Y; POOLMAN, J; THIRY, G; THONNARD, J; VOET, P; DALEMANS, W L; LHONNARD, J; DENCEL, P

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (SMIK) SMITHKLINE BEECHAM BIOLOGICALS SA

CYC 95

PI WO 2001009350 A2 20010208 (200114)* EN 127p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000068336 A 20010219 (200129)
NO 2002000506 A 20020402 (200235)
BR 2000012974 A 20020507 (200238)
CZ 2002000403 A3 20020515 (200241)
EP 1208214 A2 20020529 (200243) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2002027514 A 20020413 (200267)
HU 2002003056 A2 20021228 (200308)
CN 1377415 A 20021030 (200314)
JP 2003506049 W 20030218 (200315) 189p
MX 2002001205 A1 20030701 (200366)
ZA 2002000824 A 20031126 (200402) 130p

ADT WO 2001009350 A2 WO 2000-EP7424 20000731; AU 2000068336 A AU 2000-68336 20000731; NO 2002000506 A WO 2000-EP7424 20000731, NO 2002-506 20020131; BR 2000012974 A BR 2000-12974 20000731, WO 2000-EP7424 20000731; CZ 2002000403 A3 WO 2000-EP7424 20000731, CZ 2002-403 20000731; EP 1208214 A2 EP 2000-956369 20000731, WO 2000-EP7424 20000731; KR 2002027514 A KR 2002-701441 20020201; HU 2002003056 A2 WO 2000-EP7424 20000731, HU 2002-3056 20000731; CN 1377415 A CN 2000-813842 20000731; JP 2003506049 W WO 2000-EP7424 20000731, JP 2001-514142 20000731; MX 2002001205 A1 WO 2000-EP7424 20000731, MX 2002-1205 20020201; ZA 2002000824 A ZA 2002-824 20020130

FDT AU 2000068336 A Based on WO 2001009350; BR 2000012974 A Based on WO 2001009350; CZ 2002000403 A3 Based on WO 2001009350; EP 1208214 A2 Based on WO 2001009350; HU 2002003056 A2 Based on WO 2001009350; JP 2003506049 W Based on WO 2001009350; MX 2002001205 A1 Based on WO 2001009350

PRAI GB 1999-18319 19990803

AB WO 200109350 A UPAB: 20040107
NOVELTY - An isolated polynucleotide sequence which hybridizes under highly stringent conditions to at least a 30 nucleotide portion of 80 sequences described in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a genetically-engineered outer membrane vesicle (bleb) preparation from a Gram-negative bacterial strain characterized in that the preparation is obtainable by employing a process comprising:

(a) introducing a heterologous gene, optionally controlled by a strong promoter sequence, into the chromosome by homologous recombination; and

(b) making blebs from the strain;

(2) a vaccine comprising a bleb preparation and a pharmaceutically acceptable excipient;

(3) a vector suitable for performing recombination events;

(4) a modified Gram-negative bacterial strain from which the bleb

preparation is made;

(5) an immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell vaccine suitable for paediatric use.

ACTIVITY - Antiviral; Antibacterial; Antifungal.

Animals were immunized three times with 5 micro g of the different OMVs absorbed on Al(OH)3 on days 0, 14, and 28. Bleedings were done on days 28 and 35, and they were challenged on day 35. The challenge dose was 20 X LD50 (approx. 10 to the power of 7 CFU/mouse). Mortality rate was monitored for 7 days after challenge.

OMVs injected were:

Group1: Cps-, PorA+

Group2: Cps-, PorA-

Group3: Cps-, PorA-, NspA+

Group4: Cps-, PorA-, Omp85+

Group5: Cps-, PorA-, Hsf+

24 hours after the challenge, there was 100% mortality in the negative control group, while mice immunized with the 5 different OMVs preparations were still alive. Sickness was also monitored during the 7 days and the mice immunized with the NSPA over-expressed blebs appeared to be less sick than the other groups. PorA present in PorA+ blebs is likely to confer extensive protection against infection by the homologous strain. However, protection induced by PorA-up-regulated blebs is likely to be due at least to some extent, to the presence of increased amount of NspA, OMP85 or Hsf.

MECHANISM OF ACTION - Vaccine.

USE - The claimed polynucleotide sequence is used in performing a homologous recombination event within 1000 base pairs upstream of a Gram-negative bacterial chromosomal gene in order to either increase or decrease expression of the gene. The bleb preparation is useful in the manufacture of a medicament for immunizing a human host against a disease caused by infection of one or more of the following: Neisseria meningitidis, Neisseria gonorrhoeae, Haemophilus influenza, Moraxella catarrhalis, Pseudomonas aeruginosa, Chlamydia trachomatis, and Chlamydia pneumonia. The invention is useful for immunizing a human host against the diseases caused by the above. The invention also provides immunization against the influenza virus. Immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell vaccines are useful for paediatric use (all claimed).

ADVANTAGE - The vaccine is more immunogenic, less toxic, and safer.

Dwg.0/17

TECH UPTX: 20010312

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: A genetically-engineered outer membrane vesicle (bleb) preparation from a Gram-negative bacterial stain characterized in that the preparation is obtainable by employing one or more processes selected from:

(a) reducing immunodominant variable or non-protective antigens within the bleb preparation comprising the steps of determining the identity of such antigen, engineering a bacterial strain to produce less or non of the antigen, and making blebs from the strain;

(b) upregulating expression of protective outer membrane **proteins** (OMP) antigens within the bleb preparation comprising the steps of identifying such antigen, engineering a bacterial strain so as to introduce a stronger promoter sequence upstream of a gene encoding the antigen such that the gene is expressed at a level higher than in the non-modified bleb, and making blebs from the strain;

(c) upregulating expression of conditionally-expressed, protective OMP antigens within the bleb preparation comprising the steps identifying such an antigen, engineering a bacterial strain so as to remove the repressive control mechanisms of its expression, and making blebs from the strain;

(d) modifying lipid A portion of bacterial LPS within the bleb

preparation, comprises identifying a gene involved in rendering the lipid A portion of LPS toxic, engineering a bacterial strain so as to reduce or switch off expression of the gene, and making blebs from the strain;
(e) modifying lipid A portion of bacterial LPS within the bleb preparation, comprises identifying a gene involved in rendering the lipid A portion of LPS less toxic, engineering a bacterial stain so as to introduce a stronger promoter sequence upstream of the gene such that the gene is expressed at a level higher than in the non-modified bleb, and making blebs from the strain;
(f) reducing lipid A toxicity within the bleb preparation and increasing the levels of protective antigens, comprises engineering the chromosome of a bacterial strain to incorporate a gene encoding a Polymixin A **peptide**, or a derivative or analogue of it, fused to a protective antigen, and making blebs from the strain; or
(g) creating conserved OMP antigens on the bleb preparation comprises the steps of identifying such antigen, engineering a bacterial strain so as to delete variable regions of a gene encoding the antigen, and making blebs from the strain; where one or more of the following processes may further be employed:
(h) reducing expression within the bleb preparation of an antigen which shares a structural similarity with a human structure and may be capable of inducing an auto-immune response in humans, comprises identifying a gene involved in the biosynthesis of the antigen engineering a bacterial strain so as to reduce or switch off expression of the gene; and making blebs from the strain; or
(i) upregulating expression of protective OMP antigens within the bleb preparation comprises the steps of identifying such antigen, engineering a bacterial strain so as to introduce into the chromosome one or more further copies of a gene encoding the antigen controlled by a heterologous, stronger promoter sequence, and making blebs from the strain.
The engineering steps of (a)-(e) and (h)-(i) are carried out by homologous recombination events between a sequence of at least 30 nucleotides on the bacterial chromosome, and a sequence of at least 30 nucleotides on a vector transformed within the strain. The engineering steps are carried out by double cross-over homologous recombination events between two sequences of at least 30 nucleotides on the bacterial chromosome separated by nucleotide sequence 'X', and two sequences of at least 30 nucleotides on a vector transformed within the strain separated by nucleotide sequence 'Y', where during the recombination event X and Y are interchanged. The two nucleotide sequences are of approximately the same length and the vector is linear **DNA** molecule. (a)-(e) and (h) are carried out within the region of the chromosome 1000 base pairs upstream of the initiation codon of the gene of interest. In (a), (d), and (h) nucleotide sequence X comprises part of the promoter region of the gene, and nucleotide sequence Y comprises either a weak promoter region, or no promoter region. In (b) or (e) nucleotide sequence Y comprises a strong promoter region for the bacterium. Y is inserted 200-600 base pairs, preferably 400 base pairs, upstream of the initiation codon of the gene of interest. In (c) nucleotide sequence X comprises part of the repressive control sequence of the promoter, and Y comprises no such sequence. The recombination events in (a), (d), and (h) are carried out such that nucleotide sequence X comprises part of the coding sequence of the gene of interest. The recombination events of (i) is carried out such that Y comprises the further copy of the gene within an expression cassette.
The bleb preparation is preferably isolated from a modified Neisseria meningitidis B strain. Bleb is obtainable by employing at least (b) and/or (i) where one or more of the following genes are upregulated: NspA, Hsf-like, Hap, PorA, PorB, ONP85, PilQ, PldA, FrpB, TbpA, TbpB, FrpA, frpC, LpbA, LbpB, GhaB, HasT, lipo02, Tbp2 (lipo28), MltA (lipo30), and

ctrA.
In (a) one or more of the following genes are downregulated from: PorA, PorB, PilC, TbpA, TbpB, LbpA, LbpB. Opa, and Opc.
In (d) one or more of the following genes are downregulated from: htrB, msbB and lpxK.
In (e) one or more of the following are upregulated: pmrA, pmrB, pmrE, and pmrF.
In (c) the repressive control sequence of the promoter is the fur operator region of either or both the TbpB or LbpB genes.
In (h) one or more of the following genes are down regulated: galE, siaA, **siaB**, siaC, siaD, ctrA, ctrB, ctrC, and ctrD.
The bleb preparation may also be isolated from a modified Moraxella catarrhalis strain.
In this case in (b) and/or (i) one or more of the following genes are upregulated: OMP106, HasR, PilQ, OMP85, lipo06, lipo10, lipo11, P6, ompCD, CopB, D15, Omp1A1, Hly3, LbpA, LpbB, TbpA, TbpB, OmpE, UspA1, UspA2, and Omp21.
In (a) one or more of the following genes are down regulated: CopB, OMP106, OmpB1, TbpA, TbpB, LbpA, and LbpB.
In (d) one or more of the following genes are downregulated: htrB, msbB, and lpxK.
In (e) one or more of the following genes are upregulated: pmrA, pmrB, pmrE, and pmrF.
The bleb preparation may also be isolated from Haemophilus influenzae.
In this case in (b) and/ or (i) one or more of the following genes are upregulated: D15, P6, TbpA, TbpB, P2, P5, OMP26, HMW1-4, Hia, Hsf, Hap, Hin47, and Hif.
In (a) one or more of the following genes are downregulated: P2, P5, Hif, IgA1-protease, HgpA, HgpB, HMW1, HMW2, Hxu, TbpA, and TbpB.
In (d) one or more of the following genes are downregulated: htrB, msbB, IpxK.
In (e) one or more of the following genes are upregulated: pmrA, pmrB, pmrE, and pmrF.
The Gram-negative strain may be Neisseria gonorrhoeae, Haemophilus influenzae, or Moraxella catarrhalis and the heterologous gene is a protective OMP from Chlamydia trachomatis, Moraxella catarrhalis, and Haemophilus influenzae respectively.
Preferred Vaccine: The vaccine may be a menigococcal vaccine comprising the bleb preparation and one or more plain or **conjugated** menigococcal capsular polysaccharides selected from the serotypes A, C, Y or W. The vaccine may be a meningitis vaccine comprising the preparation, a **conjugated** H. influenzae b capsular polysaccharide, and one or more plain or **conjugated** pneumococcal capsular polysaccharides.
The vaccine may be a otitis media vaccine comprising the bleb preparation and one or more plain or **conjugated** pneumococcal capsular polysaccharides, and one or more antigens that can protect a host against non-typeable H. influenzae infection. The latter additionally comprises one or more **protein** antigens that can protect a host against Streptococcus pneumoniae and/or one or more antigens that can protect a host against RSV and/or one or more antigens that can protect a host against influenza virus.
Preferred Nucleotide: The nucleotide comprises at least 30 nucleotides, preferably at least 30 nucleotides from one of 80 sequences described in the specification of complements of them.

L35 ANSWER 14 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-071273 [08] WPIDS
DNN N2001-053932 DNC C2001-019975
TI Siah-Mediated Degradation Protein, useful for drug screening, for therapeutic applications and for functional genomics.

DC B04 D16 P14 S03
IN MATSUZAWA, S; REED, J C
PA (BURN-N) BURNHAM INST
CYC 94
PI WO 2000077207 A2 20001221 (200108)* EN 121p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000057303 A 20010102 (200121)
EP 1185652 A2 20020313 (200225) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003502042 W 20030121 (200308) 127p
US 6638734 B1 20031028 (200372)#
ADT WO 2000077207 A2 WO 2000-US15873 20000609; AU 2000057303 A AU 2000-57303 20000609; EP 1185652 A2 EP 2000-942718 20000609, WO 2000-US15873 20000609; JP 2003502042 W WO 2000-US15873 20000609, JP 2001-503651 20000609; US 6638734 B1 Provisional US 1999-367334P 19990611, US 2000-591694 20000609
FDT AU 2000057303 A Based on WO 2000077207; EP 1185652 A2 Based on WO 2000077207; JP 2003502042 W Based on WO 2000077207
PRAI US 1999-330517 19990611; US 2000-591694 20000609
AB WO 200077207 A UPAB: 20010207
NOVELTY - Isolated nucleic acid (I) encoding a Siah-Mediated Degradation Protein (SMDP) and/or Skp1 Cullin F-box (SCF)-complex protein (SCP), or their functional fragment, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vector (II) and a recombinant cell (III), containing (I);

(2) an **oligonucleotide** (Ia) comprising at least 15 nucleotides capable of specifically hybridizing to a nucleotide sequence (S1) comprising 1274, 1432, 1413, 1673, 1892, 1075 or 2037 nucleotides fully defined in the specification;

(3) an antisense-nucleic acid (Ib) capable of specifically binding to mRNA encoded by (I);

(4) a kit for detecting the presence of SMDP and/or SCP cDNA sequence, comprising (Ia);

(5) an isolated SMDP and/or SCP characterized by its ability to bind at least one SMDP and/or SCP;

(6) expressing SMDP and/or SCP;

(7) an isolated anti-SMDP and/or SCP antibody (Ab) having specific reactivity with SMDP and/or SCP;

(8) a composition comprising (Ib) effective to inhibit expression of human SMDP and/or SCP and an acceptable hydrophobic carrier capable of passing through a cell membrane;

(9) a transgenic non-human mammal expressing (I);

(10) identifying (I) by contacting a sample containing nucleic acid with (Ia) under high stringency hybridization conditions, and identifying the compounds that hybridize;

(11) detecting the presence of human SMDP and/or SCP in a sample by contacting a test sample with Ab and detecting the presence of Ab-SMDP and/or SCP complex to detect the presence of SMDP and/or SCP in the sample;

(12) single strand **DNA** primers for amplification of (I), comprising a nucleic acid sequence derived from S1;

(13) a bioassay for evaluating whether test compounds are capable of acting as agonists or antagonists for SMDP and/or SCP protein or their functional fragments, involving culturing of cells containing (I) in the

presence of a test compound whose ability to modulate activity of SMDP and/or SCP such as protein:protein binding activity or protein degradation activity, is sought to be determined, and monitoring the cells for either an increase or decrease in the level of protein activity;

(14) a therapeutic composition (TC) comprising SMDP and/or SCP, their functional fragments, a compound identified the above said method, or Ab;

(15) inducing the degradation function of a target protein, by expressing a chimeric protein (CP) comprising a target-protein binding domain operatively **linked** to a protein degradation binding domain of a protein unit of the ubiquitin-mediated protein degradation family, in a cell;

(16) determining the function of a target protein, by expressing CP in a first cell, and comparing its phenotype to the phenotype of a control second cell;

(17) identifying a nucleic acid molecule encoding a protein that modulates a cellular phenotype, by expressing a chimeric nucleic acid comprising a unit of nucleic acid library fused to nucleic acid encoding a protein degradation binding domain of a protein unit of the ubiquitin-mediated protein degradation family, in a cell, and screening the cell for the modulation of the phenotype;

(18) a chimeric nucleic acid screened by the above said method;

(19) a nucleic acid library comprising a number of chimeric nucleic acids such that each chimeric nucleic acid comprises an SMDP and/or SCP or its functional fragment;

(20) treating a disease by degrading the function of a target protein, by introducing CP into a cell; and

(21) a chimeric protein comprising SMDP and/or SCP.

ACTIVITY - Cytostatic; antiinflammatory; antiarthritic; immunosuppressive; antibacterial.

No supporting data given.

MECHANISM OF ACTION - Modulator of SMDP and/or SCP activity.

No supporting data given.

USE - SMDP and/or SCP are useful for modulating the activity of oncogenic proteins. Agonists or antagonists of SMDP and/or SCP protein are useful for modulating the activity of SMDP and/or SCP protein as well as modulating protein degradation mediated by SMDP and/or SCP protein. TC is useful for treating a pathology characterized by abnormal cell proliferation and inflammation. (I) is useful as a probe for assaying the presence and/or the amount of SMDP and/or SCP gene or mRNA transcript in a given sample. (I) and (Ia) are also useful as primers and/or templates in PCR (polymerase chain reaction) for amplifying (I). SMDP and/or SCP proteins are useful in bioassays, and as immunogens for producing Ab. Bioassays are useful for monitoring SMDP and/or SCP levels and for diagnosing physiological disorders that result from abnormal levels of SMDP and/or SCP. SMDP and/or SCP are useful for treating cancer pathologies, keratin hyperplasia, keloid, neoplasia, benign prosthetic hypertrophy, inflammatory hyperplasia, bone marrow aplasia, immunodeficiencies and inflammatory diseases such as sepsis, fibrosis, arthritis and graft versus host diseases.

Dwg.0/10

TECH UPTX: 20010207

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Sequence: (I) comprises a **DNA** encoding an amino acid sequence comprising 298, 228, 80, 443, 522, 327 or 447 amino acids fully defined in the specification, a **DNA** that hybridizes to the above **DNA** under moderately stringent conditions and encoding biologically active SMDP and/or SCP, or a **DNA** degenerate with respect to either of the above sequences and encoding a biologically active SMDP and/or SCP. (I) comprises a sequence that hybridizes under high stringent conditions to the SMDP and/or SCP coding portion of S1. (Ia) is labeled with detectable marker.

Ab is a monoclonal or polyclonal antibody. (I) is **Sia**-1alpha, SIP-L, SIP-S, SAF-1, SAF-2, and SAD, or their functional fragments. Preferred Method: (I) has been mutated and SMDP and/or SCP so expressed is not native to SMDP and/or SCP. Activity of SMDP and/or SCP is modulated by binding of Siah-1 to APC. The transgenic non-human animal expressing (I) is a mouse. (I) which modulates the phenotype such as cell proliferation, cell survival, cell death, cell secretion or cell migration, is screened.

L35 ANSWER 15 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-549134 [50] WPIDS
DNC C2000-163952
TI Novel polypeptides containing pIgR-binding domains used for targeting and transport to the mucosal epithelia, in the treatment of disorders accessible to the mucosal epithelia, e.g. asthma.
DC B04 D16
IN CAPRA, J D; HEXHAM, J M; MANDECKI, W; WHITE, K
PA (DGIB-N) DGI BIOTECHNOLOGIES; (OKLA-N) OKLAHOMA MEDICAL RES FOUND; (TEXA) UNIV TEXAS SYSTEM; (DGIB-N) DGI BIOTECHNOLOGIES INC
CYC 91
PI WO 2000047611 A2 20000817 (200050)* EN 137p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000027597 A 20000829 (200062)
EP 1151000 A2 20011107 (200168) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002539771 W 20021126 (200307) 166p
AU 769259 B 20040122 (200412)
ADT WO 2000047611 A2 WO 2000-US3650 20000211; AU 2000027597 A AU 2000-27597 20000211; EP 1151000 A2 EP 2000-906030 20000211, WO 2000-US3650 20000211; JP 2002539771 W JP 2000-598527 20000211, WO 2000-US3650 20000211; AU 769259 B AU 2000-27597 20000211
FDT AU 2000027597 A Based on WO 2000047611; EP 1151000 A2 Based on WO 2000047611; JP 2002539771 W Based on WO 2000047611; AU 769259 B Previous Publ. AU 2000027597, Based on WO 2000047611
PRAI US 1999-119932P 19990212
AB WO 200047611 A UPAB: 20001010
NOVELTY - A 10-50 residue peptide (I) comprising a pIgR-binding domain, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a fusion protein comprising a pIgR-binding domain covalently **linked** to a non-antibody peptide or polypeptide;

(2) a polynucleotide encoding the fusion protein of (1);

(3) targeting an agent to a mucosal epithelium comprising administering to a mammal a targeting complex comprising the agent and (I), the complex binds to, and is taken up by, cells expressing pIgR, and is transported to the mucosal epithelium;

(4) targeting a non-antibody peptide or polypeptide to a mucosal epithelium, comprising administering the fusion protein of (1) to a mammal, the protein binds to, and is taken up by, cell expressing pIgR, and is transported to the mucosal epithelium;

(5) delivering an agent to a cell, comprising contacting (I) with a cell expressing pIgR; and

(6) delivering a non-antibody peptide or polypeptide to a cell, comprising contacting the fusion protein of (1) with a cell expressing

pIgR.

ACTIVITY - Antiasthmatic; antiinflammatory; antiinfectious; cytostatic; antiulcer; antidiarrheal; hepatropic; virucide; vasotropic; anti-human immunodeficiency virus; antibacterial. No biological data is given.

MECHANISM OF ACTION - None given.

USE - For targeting and transport to the mucosal epithelium (claimed), for the prevention or treatment of diseases, ailments or conditions that are accessible to mucosal epithelia, including asthma, bronchitis, emphysema, cystic fibrosis, bronchiectasis, bronchiolitis, pulmonary edema, viral tracheobronchitis, sleep apnea syndrome, infectious diseases, neoplastic conditions, Loffler's syndrome, kyphocliosis, dysphagia, peptic ulcers, diarrheal diseases, ulcerative colitis, Crohn's disease, hepatitis, cirrhosis, hemorrhoids, systemic vasculitis, acquired immunodeficiency syndrome, gonorrhea, syphilis and chlamydia. (I) can be attached to a detectable label for use in diagnostics.

Dwg.0/8

TECH UPTX: 20001010

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Peptide: (I) is 10, 15, 20, 25, 30, 35, 40, 45 or 50 residues in length, and further comprises a **linking** moiety, preferably SMTP, SPDP, LC-SPDP, Sulfo-LC-SDPD, **SMCC**, Sulfo-**SMCC**, **MBS**, Sulfo-**MBS**, **SIAB**, Sulfo-**SIAB**, SMPM, Sulfo-**SMPB**, EDC/Sulfo-NHS, or ABH, attached to the peptide. The **linking** moiety may be further attached to an agent, preferably a peptide, polypeptide, **oligonucleotide**, polynucleotide, detachable label or drug. The polypeptide is an enzyme, antibody region, region mediating protein-protein interaction, cytokine, growth factor, hormone, toxin, tumor suppressor, transcription factor, or apoptosis inducer. The polynucleotide encodes a polypeptide, a single chain antibody, an antisense construct or a ribozyme. The detectable label is rhodamine, fluorescein, green fluorescent protein or a radiolabel. The drug is an antibiotic, **DNA** damaging agent, enzyme inhibitor, or metabolite. Alternatively, (I) further comprises a non-pIgR targeting agent **linked** to the peptide. The targeting agent is an antigen binding domain of an antibody, a receptor ligand or ligand binding domain. (I) may comprise two pIgR-binding domains, and further comprise the **linking** agent and the agent.

Preferred Fusion Protein: The domain is Calpha3 domain. The non-antibody peptide or polypeptide is an enzyme, antibody region, region mediating protein-protein interaction, cytokine, growth factor, hormone, toxin, tumor suppressor, transcription factor, or apoptosis inducer.

Preferred Complex: The targeting complex further comprises a non-pIgR targeting agent.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Prior to performing the method of (5), the cell is transformed with an expression construct encoding pIgR under the control of a promoter.

Preparation: (I) can be produced by standard recombinant techniques.

L35 ANSWER 16 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2000-222357 [19] WPIDS

DNC C2000-067814

TI New dendritic polymer has a core containing a disulfide group, useful in diagnostics, drug delivery, gene therapy, magnetic resins imaging and in detection of ions and molecules.

DC A23 A26 A96 B04 D16 J04

IN BROTHERS, H M; CHENG, R C; HSU, Y; KLIMASH, J W; SPINDLER, R; SWANSON, D R; TOMALIA, D A; YIN, R

PA (DEND-N) DENDRITECH INC

CYC 1
PI US 6020457 A 20000201 (200019)* 42p
ADT US 6020457 A Provisional US 1996-24734P 19960930, US 1997-941527 19970930
PRAI US 1996-24734P 19960930; US 1997-941527 19970930
AB US 6020457 A UPAB: 20000419
NOVELTY - A dendritic polymer (I) with a core containing a disulfide group and at least two dendrons emanating from the core, each dendron having at least two terminal groups, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a thin film coated substrate (II) comprising a substrate which has been subjected to application of ions or ionizable compounds of the same charge over its surface and one or more layers of organic materials which in each layer contains ions of the same charge, the ions of the layer immediately adjacent to the substrate have the opposite charge to the modified substrate and each further layer has a charge opposite that of the previous layer and at least one of the layers comprises a dendritic polymer;

(2) a quartz crystal electrode comprising a metal coated quartz crystal electrode coated with a dendritic polymer;

(3) a differentiated dendritic polymer (III) having a core with a disulfide group and at least 2 dendrons with at least 2 terminal groups emanating from the core where at least one of the dendrons has terminal groups which are different from those of the other dendron;

(4) a method (A) of making (I) comprising reacting the terminal groups of the core molecule with the dendrons so the single reactive groups present on the dendrons bond to one of the terminal reactive groups of the core molecule;

(5) a method (B) of making (II) comprising applying one or more layers of organic molecules from a solution to the substrate to be coated;

(6) a method (C) of making (III) comprising providing first and second dendritic polymers (I), combining and subjecting the first and second polymers to reducing conditions to form a mixture of two different types of (I) each having a single reactive sulfhydryl group and subjecting the mixture to aerobic, oxidizing conditions to form a mixture containing the first and second polymers and a differentiated dendritic polymer comprised of a part of each of the original first and second polymers;

(7) a gel (IV) comprised of **crosslinked** dendritic polymers which have sulfhydryl terminal groups that react with sulfhydryl terminal groups of another dendritic polymer to form a **crosslinked** gel; and

(8) a dendritic polymer conjugate (V) comprising a dendritic polymer which has a sulfhydryl group and a first carried material which has a sulfhydryl-reactive group, conjugated to the polymer at the sulfhydryl group.

USE - The dendritic polymers are useful in diagnostics, drug delivery, gene therapy, magnetic resins imaging and in detection of ions and molecules.

Dwg.0/26

TECH UPTX: 20000419
TECHNOLOGY FOCUS - POLYMERS - Preferred Core: The core is a polyamine compound containing a disulfide group. The polyamine compound is preferably a diamine, especially cystamine.
Preferred Dendrons: The dendrons are polyamidoamine dendrons. Each of the dendrons has branch arms which include a disulfide group which is inert under non-reducing conditions but which will react with a reducing agent to form a dendritic polymer having sulfhydryl terminal groups. The disulfide groups comprise the terminal groups of the branch arms. The differentiated dendritic polymer has at least one of the dendrons with terminal groups different from those of the other dendron, the first

dendron is of a different generation to the second dendron.
Preferred Method (A): The terminal groups of the core molecule are reacted with a first reagent to form a -one half generation dendrimer. Each molecule of the reagent has at least a single reactive site which bonds with one of the reactive terminal groups of the core molecule and at least one reactive group which becomes a terminal reactive group on the -one half generation dendrimer. Each of the terminal reactive groups on the -one half generation dendrimer are reacted with a second reagent to form a zero generation dendrimer. Each molecule of the second reagent includes at least one reactive site which bonds with a terminal reactive group on the -one half generation dendrimer and at least one reactive site which becomes a terminal reactive group on the zero generation dendrimer. Additional reagents can be employed to synthesize a dendritic polymer of a desired generation. An iterative excess reagent technique, alternately employing excess amounts of methyl acrylate and ethylene diamine can be used.
Preferred Electrode: The polymer coating of the quartz crystal electrode comprises a monolayer of dendritic polymer molecules.
Preferred Gel: (IV) comprises dendritic polymers which have **amine** terminal **groups** and iminothiolane, preferably a polyamidoamine dendrimer, and are prepared by subjecting a dendritic polymer with **sulfide groups** to oxidizing conditions. (IV) can be resolubilized by adding a reducing agent such as dithioreitol to provide a redox reversible gel.
Preferred Carried Materials: (V) includes surface functional groups with a second carried material **conjugated** to them. At least one of the first and second carried materials is a bioactive agent which is a pharmaceutical agent, drug, pharmaceutical intermediary, radioprotective agent, toxin, antibody, antibody fragment, hormone, biological responses modifier, scavenging agent, **polypeptide** and/or **protein** . Preferably at least one of the first and second carried materials is an **oligonucleotide.** The second carried material is a bioactive agent and/or a signal amplifier and is preferably triethyltinpropanate.

L35 ANSWER 17 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-633734 [54] WPIDS
CR 1999-602308 [52]
DNN N1999-467958 DNC C1999-185059
TI Compositions of matter comprising photoluminescent compound, have excitation and emission spectra in inaccessible regions of spectrum e.g. red and near infrared.
DC B02 B04 D16 E24 G04 J04 S03
IN TERPETSCHNIG, E A; OSWALD, B; PATSENKER, L D
PA (TERP-I) TERPETSCHNIG E A
CYC 87
PI WO 9951702 A1 19991014 (199954)* EN 80p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9933863 A 19991025 (200011)
EP 1078023 A1 20010228 (200113) EN
R: AT BE CH DE DK ES FI FR GB IE IT LI LU NL SE
US 6538129 B1 20030325 (200325)
ADT WO 9951702 A1 WO 1999-US7627 19990407; AU 9933863 A AU 1999-33863 19990407; EP 1078023 A1 EP 1999-915319 19990407, WO 1999-US7627 19990407; US 6538129 B1 Cont of WO 1999-US7627 19990407, US 2000-684627 20001006
FDT AU 9933863 A Based on WO 9951702; EP 1078023 A1 Based on WO 9951702

PRAI US 1998-83820P 19980501; DE 1998-19815659 19980408; US 2000-684627 20001006

AB WO 9951702 A UPAB: 20030516

NOVELTY - Compositions of matter comprising photoluminescent compound.

DETAILED DESCRIPTION - Photoluminescent compound is of formula (I): Z = 4-6-membered aromatic ring; A-F are substituents of Z, F = absent when Z = 5-membered ring and E, F are absent when Z = 4-membered ring; A-F may be present in any order provided that B and C are adjacent, in which case A, D-F is neutral or provided that B and C are separated by one of A, D-F in which case one of A, D-F is negatively charged; A = S, Se, Te or C(Ra)(R); and B, C = W1, W2. Full definitions are provided in the Definitions (Full definitions) Field. INDEPENDENT CLAIMS are also included for (1) method of performing photoluminescence assay; and (2) method of synthesizing photoluminescent compounds.

USE - Used to perform photoluminescence assays (claimed). Used in spectroscopy, microscopy, immunoassays and hybridization assays, in free and **conjugated** forms as probes, labels and indicators, in competitive assays that include recognition groups, binding partners or analytes such as biomolecules, polymers and drugs, in immunoassays such as sandwich assays using secondary antibodies, binding between avidin and biotin, **protein** A and immunoglobulins, lectins and sugars (concanavalin A and glucose), to sequence nucleic acids and **peptides**, e.g. to trace **DNA** fragments, for fluorescence in situ hybridization methods, for single nucleotide applications and for screening assays for combinatorial libraries of compounds.

ADVANTAGE - Have excitation and emission spectra in relatively inaccessible regions of spectrum including red and near infrared. Multicolor labeling allows different biochemical parameters to be monitored simultaneously.

DESCRIPTION OF DRAWING(S) - Excitation (dotted line) and emission (solid line) spectra for (13)-human serum albumin (HAS) in phosphate buffered saline.

Dwg.1/1

TECH UPTX: 19991221

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred compositions - Compositions further comprise carrier associated non-covalently with the photoluminescent compound or covalently through reaction with a reactive group on at least one Z. Compositions further comprise luminophores or chromophores. One of the photoluminescent compound and second compound is an energy transfer donor and the other is an energy transfer acceptor. Preferred photoluminescent compound - Z is based on squaric acid, croconic acid or rhodizonic acid. At least one of Z = reactive group, preferably chosen for reacting with **amine groups** (N-hydroxysuccinimide esters, isothiocyanates or sulfonylhalogenides), **thio groups** (iodoacetamides or maleimides) or nucleic acids (phosphoamidites) or = **linked** carrier, preferably **polypeptide**, polynucleotide, bead, microplate well surface or other solid surface. At least one substituent of Z is an ionic substituent capable of increasing the hydrophilicity of the entire photoluminescent compound, preferably SO3-, COO Or n(RI)+ (RI = aliphatic or aromatic group). Photoluminescent compound is suitable for excitation in the red or near infrared range. Photoluminescent compound is capable of emitting light with wavelength of 600-900 nm. Photoluminescent compound has a Stokes' shift of at least about 5 nm. Photoluminescent compound is capable of covalently reacting with biological cells, **DNA**, lipids, nucleotides, polymers, **proteins** and/or pharmacological agents. Photoluminescent compound is asymmetric or symmetric about Z. Photoluminescent compound may be induced to luminesce by exposing it to electromagnetic, chemical and or electrochemical energy.

L35 ANSWER 18 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-430042 [36] WPIDS
DNC C1999-126684
TI Determining sequence of a nucleic acid by mass spectrometry.
DC B04 C06 D16 J04
IN CANTOR, C; KANG, C; KIM, Y T; KOESTER, H; KWON, Y; LITTLE, D P; LOUGH, D M; O'DONNELL, M J; XIANG, G; CANTOR, C R; KIM, Y; ODONNELL, M J; LITTLE, M J
PA (KOAD) KOREA ADV INST SCI & TECHNOLOGY; (ODON-I) O'DONNELL M J; (SEQU-N) SEQUENOM INC
CYC 85
PI WO 9931278 A1 19990624 (199936)* EN 116p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9919187 A 19990705 (199948)
EP 1038031 A1 20000927 (200048) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2000003058 A 20000815 (200052)
US 6268131 B1 20010731 (200146)
KR 2001033130 A 20010425 (200164)
JP 2002508192 W 20020319 (200222) 159p
AU 745149 B 20020314 (200231)
JP 3331210 B2 20021007 (200273) 50p
EP 1038031 B1 20031126 (200402) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 69820111 E 20040108 (200411)
ADT WO 9931278 A1 WO 1998-US26718 19981215; AU 9919187 A AU 1999-19187 19981215; EP 1038031 A1 EP 1998-963969 19981215, WO 1998-US26718 19981215; NO 2000003058 A WO 1998-US26718 19981215, NO 2000-3058 20000614; US 6268131 B1 US 1997-990851 19971215; KR 2001033130 A KR 2000-706503 20000614; JP 2002508192 W WO 1998-US26718 19981215, JP 2000-539175 19981215; AU 745149 B AU 1999-19187 19981215; JP 3331210 B2 WO 1998-US26718 19981215, JP 2000-539175 19981215; EP 1038031 B1 EP 1998-963969 19981215, WO 1998-US26718 19981215; DE 69820111 E DE 1998-620111 19981215, EP 1998-963969 19981215, WO 1998-US26718 19981215
FDT AU 9919187 A Based on WO 9931278; EP 1038031 A1 Based on WO 9931278; JP 2002508192 W Based on WO 9931278; AU 745149 B Previous Publ. AU 9919187, Based on WO 9931278; JP 3331210 B2 Previous Publ. JP 200208192, Based on WO 9931278; EP 1038031 B1 Based on WO 9931278; DE 69820111 E Based on EP 1038031, Based on WO 9931278
PRAI US 1997-990851 19971215
AB WO 9931278 A UPAB: 19990908
NOVELTY - A new method for determining the sequence of a target nucleic acid molecule comprises transcribing the nucleic acid molecule which has a promoter, followed by determining the molecular weight of the transcripts by mass spectrometry.

DETAILED DESCRIPTION - A new method for determining the sequence of a target nucleic acid molecule comprises:

(a) providing a nucleic acid molecule comprising a promoter and target nucleic acid sequence operatively **linked** to the promoter, where the nucleic acid molecule is immobilized on a solid support;

(b) transcribing the promoter-containing nucleic acid molecule with an RNA polymerase that recognizes the promoter under conditions where a nested set of RNA transcripts from the target is produced; and

(c) determining the molecular weight of the transcripts by mass spectrometry and therefore determining the nucleic acid sequence of the target molecule.

An INDEPENDENT CLAIM is also included for a method of identifying transcriptional terminator or attenuator sequences comprising:

(a) immobilizing a nucleic acid promoter containing probe on a solid support, where the nucleic acid promoter containing probe comprises at least 5 nucleotides at the X-end of the coding strand that is complementary to a single stranded region at the X-end of the target nucleic acid;

(b) hybridizing the nucleic acid to be sequenced to the immobilized nucleic acid probe;

(c) transcribing the target nucleic acid with an RNA polymerase to produce a sequence-terminated RNA transcript, where the RNA polymerase recognizes the promoter; and

(d) determining the molecular weight value of the RNA transcript by mass spectrometry, where the terminator sequence or attenuator is identified.

USE - The method is used for sequencing nucleic acids by mass spectrometry. In particular, the method can be used to identify transcriptional terminator or attenuator sequences (claimed). Rho-dependent and rho-independent terminators may be detected by the method.

ADVANTAGE - The array format comprising high densities of nucleic acid probes facilitates mass spectrometric detection. RNA fragments are more stable during matrix-assisted laser desorption/ionization (MALDI) mass spectrometry than **DNA** fragments. This may be a result of the 2'-hydroxyl group on the sugar moiety of RNA, which helps to reduce depurination during the MALDI process. Ribonucleoside triphosphate analogues are used in the method, so that the resulting RNA transcripts have reduced secondary structure, or the fidelity of termination and turnover of the RNA polymerase enzyme is increased compared to RNA transcripts formed from ribonucleoside triphosphates.

Dwg.0/17

TECH UPTX: 19990908

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The promoter-containing nucleic acid molecule is immobilized by the 5' end of the coding strand or the 3' end of the non-coding strand. The nucleic acid is **DNA** or peptide nucleic acid (PNA). The nucleic acid molecule comprising a promoter and target is prepared by hybridizing a promoter-containing probe having a coding and non-coding strand to a nucleic acid molecule comprising a target sequence, where hybridization occurs between a single-stranded region of the promoter-containing probe and a complementary single-stranded region at one end of the molecule comprising the target. The target is single-stranded and the complementary sequence is at the 3' end. The double-stranded promoter-containing probe comprises a single-stranded region of at least 5 nucleotides at the 3' end of the coding strand that are complementary to the corresponding target sequence.

Alternatively, the target is double-stranded except for an at least 5 contiguous nucleotide single-stranded region that is complementary to the corresponding portion of the probe and the single-stranded portion of the promoter containing molecule is at the same end, relative to the promoter, such that the single-stranded region is on the target containing molecule. The promoter containing molecule is immobilized on the solid support prior to hybridization of the target containing molecule. Alternatively, the hybridization may be performed prior to immobilization of the promoter containing molecule on the solid support.

Nicks in the resulting molecules are ligated prior to transcription by the RNA polymerase. RNA polymerase is used to transcribe the promoter-target

nucleic acid to produce several base-specifically-terminated RNA transcripts. The RNA transcripts may be specifically cleaved with base-specific ribonucleases to produce a set of cleaved fragments whose weight values are assessed by mass spectrometry. The sequence of all or a part of the target is determined by the RNA transcripts according to the molecular weight. The nucleic acid molecule comprising the promoter is produced by immobilizing a single-stranded molecule that comprises a promoter or the complement of a promoter and hybridizing a fragment that comprises its complement, where the resulting molecule comprises a double-stranded region containing a promoter and a single-stranded portion of at least 5 nucleotides. The promoter is an archaebacteria, eubacteria, bacteriophages, **DNA** viruses, RNA viruses, plants, plant viruses or animal promoters.

Hybridization of the target and promoter-containing molecules results in the formation of a nick in the coding strand corresponding to positions beyond +6 relative to the start of transcription from the promoter. The nick is preferably at position +7, +8, +9 or +19 positions.

Prior to immobilization of the nucleic acid, the surface of the support is derivatized, by reaction of the surface with an aminosilane, e.g. 3-aminopropyltriethoxysilane, to produce primary amines on the surface of the support. The primary amines are further reacted with a thiol-reactive cross-**linking** reagent, e.g. N-succinimidyl (4-iodoacetyl) aminobenzoate (**SIAB**), to form a thiol-reactive solid support.

Immobilization of the nucleic acid probe to a solid support is effected by reacting the thiol reactive solid support with a nucleic acid probe having a free 5'- or 3'-thiol group. The nucleic acid is immobilized to the surface at a density of at least 20 fmol/mm2 by a covalent **linkage** . The nucleic acids are immobilized on the surface of a solid support (e.g. silicon or silicon coated) in the form of an array. The solid surface has many wells which are pitted.

Transcription reactions are performed in the presence of a ribonucleoside triphosphate analogue, where the resulting RNA transcripts have reduced secondary structure, or the fidelity of termination and turnover of the RNA polymerase enzyme is increased compared to RNA transcripts formed from ribonucleoside triphosphates. The analogues are chosen from inosine 5'-triphosphate (ITP), 4-thiouridine 5'-triphosphate (UTP), 5-bromo UTP and 5'-iodo CTP.

Transcription may be performed in the presence of one or more 3'-deoxyribonucleotides. The nucleic acid may be immobilized to the solid support via a **linker.** The **linkage** is photolabile, acid labile or chemically cleavable. A matrix material is added to the surface of the support before or after immobilization of the nucleic acid for mass spectrometry. RNA transcripts are conditioned prior to performing mass spectrometry. The RNA polymerase is a **DNA**-dependent or RNA-dependent RNA polymerase. The RNA polymerase is especially that of Escherichia coli, T7, SP6 or T3 RNA polymerase or Qbeta replicase.

L35 ANSWER 19 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-190636 [16] WPIDS
DNN N1999-139408 DNC C1999-056165
TI Detection and identification of micro-organisms - by in situ staining with a composition which degrades the cell wall to allow penetration of a probe.
DC B04 C07 D15 D16 D21 J04 S03
IN SCHUT, F; TAN, P S T
PA (MICR-N) MICROSCREEN BV
CYC 83
PI WO 9910533 A1 19990304 (199916)* EN 70p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9888904 A 19990316 (199930)

EP 1009862 A1 20000621 (200033) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT WO 9910533 A1 WO 1998-NL481 19980826; AU 9888904 A AU 1998-88904 19980826; EP 1009862 A1 EP 1998-940684 19980826, WO 1998-NL481 19980826

FDT AU 9888904 A Based on WO 9910533; EP 1009862 A1 Based on WO 9910533

PRAI EP 1997-202618 19970826

AB WO 9910533 A UPAB: 19990424

NOVELTY - Detecting and identifying micro-organisms by staining with a composition that partly degrades the cell wall or cell membrane of the micro-organism, so that a probe can penetrate the cell, is new. The probe is targeted to a sequence in the micro-organism, and is subsequently detected.

DETAILED DESCRIPTION - A method for in situ staining of micro-organisms (e.g. viruses, bacteria, yeast fungi and plant cells) comprises: (a) mixing a material containing at least one micro-organism with a composition which can (partly) degrade a cell wall or cell membrane of a micro-organism thereby allowing for penetration through the wall or membrane of a (labelled) probe; (b) reacting the probe with an antigen or nucleic acid molecule present in the cell; and (c) detecting the presence of the probe in the micro-organism. The micro-organism is optionally fixed with a fixative to further retain its corpuscular character.

INDEPENDENT CLAIMS are also included for the following: (1) a nucleic acid probe derived from a thiolated probe **linked** to horse-radish peroxidase with a sulfo-**SMCC linker**; (2) a method for **linking** a nucleic acid probe to horse-radish peroxidase (HRP), comprising mixing a thiol **oligonucleotide** with a **SMCC**-HRP complex, incubating the mixture, and purifying the probe by ultrafiltration; (3) a diagnostic test kit for use with in situ staining which comprises a cell wall degrading composition and a nucleic acid probe; and (4) an enzyme-**linked** assay or diagnostic kit which comprises the probe defined in (1).

USE - The method can be used for identification of organisms, and possibly to differentiate between strains, e.g. in cheese-making. It can also be used to measure the potential metabolic activity or level of individual enzymes. The method can be used to study mRNA activity in , e.g. fermentation cultures. The method can also be used to study the effect of novel foods, probiotics, and functional foods on intestinal microflora, to monitor the development of mixed bacterial populations in fermentation processes, e.g. cheese and other dairy fermentation, beer, wine, etc., as well as in modern biotechnology, to identify and quantify the presence and activity of micro-organisms in wastewater treatment systems and bioremediation processes, to determine the microbial status of (polluted) soils, waters, gases, potable water, swimming water and surface water. The method can also be used to detect pathogens and bacterial resistance, especially ''caries-carrying'' oral Streptococci for the toothpaste industry, and Mycobacterium tuberculosis directly in sputum samples, which cannot be detected in situ by conventional in situ fluorescence techniques.

ADVANTAGE - The method allows for controlled degradation of cell walls in combination with a detection technique, allowing for in situ staining and detection. The present method provides a signal amplification of at least 30-50 fold, and even 80 fold, as compared with conventional fluorescent probes. The method utilises short probes, instead of the long (approximately 200 bp) labelled transcripts presently used for in situ mRNA detection. The method allows direct detection of non-growing cells,

and for cells which contain low copy numbers of mRNA.
Dwg.0/8

L35 ANSWER 20 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-105092 [09] WPIDS
DNN N1999-075937 DNC C1999-031144
TI New plasmid expressing fusion protein of polypeptide and methylase - binds to methylase binding site in the plasmid forming a covalent **conjugate**, used to create libraries for screening, or in vitro evolution, of mutant peptides with altered binding properties.
DC B04 D16 S03
IN EPSTEIN, D M
PA (SCRI) SCRIPPS RES INST
CYC 1
PI US 5856090 A 19990105 (199909)* 90p
ADT US 5856090 A US 1994-305764 19940909
PRAI US 1994-305764 19940909
AB US 5856090 A UPAB: 19990302
New plasmid (A) comprises: (a) gene fusion construct (GFC) including a gene (I) for cytosine (C5) **DNA** methylase (II) covalently attached, directly or through a **linker**, to a gene (III) encoding a **polypeptide** determinant (IV), with GFC expressing a fusion of (II) and (IV); (b) a promoter operatively **linked** to the gene fusion construct for transcription of GFC to mRNA; and (c) a methylase **conjugation** element (MCE) **linked** to GFC, directly or through a **linker**, containing a methylase binding site (**MBS**) including at least one copy of a nucleotide sequence (NS) that includes a cytidine suicide analogue (CSA) binding irreversibly to and being a methylase substrate for (II) of the fusion **protein.**
Also claimed are: (1) plasmid-**polypeptide** determinant **conjugates** (PPDC) consisting of (A) covalently coupled to the fusion **protein** from GFC via a pyrimidine group of CSA; (2) libraries of PPDC; and (3) methods for obtaining a nucleic acid sequence (IIIa) encoding a **polypeptide** (IVa) that is an a altered form of wild-type (IV), using the libraries of (2).
USE - The method can be used to identify mutants of glutathione-S-transferase (GST), an important target in treatment of cancer and Schistosoma infection and can also be applied to hormones or enzymes. The method can be used to isolate low copy number wild-type proteins, provided a specific binding agent is available. The identified mutants can then be used to screen inhibitors and inactivators (potential anti-neoplastic and antimalarial agents) for their binding affinity.
ADVANTAGE - The method rapidly and efficiently **links** genetic information with the encoded protein, making repeated rounds of screening without use of a phage-display library possible. Since PPDC are covalently **linked**, they are stable, easily manipulated (e.g. affinity chromatography can be done without breaking the **link**) and are compatible with nucleic acid sequencing and amplification techniques.
Dwg.0/24

L35 ANSWER 21 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1998-216491 [19] WPIDS
DNC C1998-068600
TI Sequence independent amplification of **DNA** - without the need for prior sequence knowledge or requirements.
DC B04 D16
IN BOHLANDER, S K
PA (ARCH-N) ARCH DEV CORP
CYC 1

PI US 5731171 A 19980324 (199819)* EN 26p
ADT US 5731171 A US 1993-96637 19930723
PRAI US 1993-96637 19930723
AB US 5731171 A UPAB: 19980512
A method for the sequence independent amplification (**SIA**) of **DNA** is new. This comprises:
(a) denaturing a **DNA** sample and annealing it with a first primer (I) which has a random 3' sequence and defined 5' sequence;
(b) incubating the **DNA**-primer hybrid with a **DNA** polymerase, especially T7 **DNA** polymerase, to synthesise a product; and
(c) carrying out a low stringency, then a high stringency Polymerase Chain Reaction (PCR) on the product using a second primer (II) that has the same 3' as the first, but also has an additional 5' overhang.
USE - The method is useful for amplifying small amounts of microdissected chromosomal samples (yeast artificial chromosome (YAC), gel purified, genomic or cloned **DNA**) which do not contain any particular restriction sites or repetitive sequences and can be derived from any species or organism. The method can also be used for deriving fluorescent in situ hybridisation (FISH) labelled products which can be used to screen YACs for chromosomal translocations in human tumours.
ADVANTAGE - This method does not require any prior sample sequence knowledge. Also no prior restriction enzyme manipulation and **linker** attachment to isolate unknown sequences is required. Screening of chromosomal translocations is simplified as several reactions can be run at the same time and the chance of contamination is cut down as the number of steps and manipulations is reduced.
Dwg.0/7

L35 ANSWER 22 OF 22 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1994-279761 [34] WPIDS
DNC C1994-127735
TI Photo-protein binding reagent **conjugate** compsn. useful in diagnostic and detection assays - comprises luminescent, sulfhydryl-activated photo-protein coupled to sulphydryl-reactive binder.
DC B04 D16
IN STULTS, N L
PA (SEAL-N) SEALITE SCI INC
CYC 48
PI WO 9418342 A1 19940818 (199434)* 32p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV MG MN MW NL NO NZ PL PT RO RU SD SE SK UA VN
AU 9461718 A 19940829 (199501)
EP 683822 A1 19951129 (199601) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5486455 A 19960123 (199610) 15p
JP 08506897 W 19960723 (199650) 38p
EP 683822 A4 19971105 (199840)
IL 108607 A 19981206 (199913)
EP 683822 B1 20020502 (200230) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69430523 E 20020606 (200245)
ADT WO 9418342 A1 WO 1994-US1387 19940204; AU 9461718 A AU 1994-61718 19940204, WO 1994-US1387 19940204; EP 683822 A1 EP 1994-908734 19940204, WO 1994-US1387 19940204; US 5486455 A Cont of US 1993-17116 19930212, US 1994-293648 19940822; JP 08506897 W JP 1994-518303 19940204, WO 1994-US1387 19940204; EP 683822 A4 EP 1994-908734 19940204; IL 108607 A IL 1994-108607 19940209; EP 683822 B1 EP 1994-908734 19940204, WO 1994-US1387 19940204; DE 69430523 E DE 1994-630523 19940204, EP 1994-908734 19940204,

WO 1994-US1387 19940204
FDT AU 9461718 A Based on WO 9418342; EP 683822 A1 Based on WO 9418342; JP 08506897 W Based on WO 9418342; EP 683822 B1 Based on WO 9418342; DE 69430523 E Based on EP 683822, Based on WO 9418342
PRAI US 1993-17116 19930212; US 1994-293648 19940822
AB WO 9418342 A UPAB: 19971006
Photoprotein binding reagent **conjugate** comprises a sulphydryl activated photoprotein capable of participating in luminescent reaction to produce light, copuled to sulphydryl reactive binding reagent capable of binding specifically to analyte.

Also claimed is preparation of a photoprotein-binding reagent **conjugate** compsn. by coupling sulphydryl-activated photoprotein capable of participating in a luminescent reaction space to produce light, to sulphydryl-reactive binding reagent capable of binding specifically to analyte.

Conjugates are pref. (1) photoprotein selected from aopaequorin, aequorin, apo-obelin, obelin, apo-mnemiopsin, mnemiopsin, apo-berovin, berovin, pholasin, luciferases, bioluminescent **proteins** from Pelagia, or ostracods; and (2) binding reagent selected from streptavidin/avidin, lectins, enzymes, glycoproteins, **peptides**, hormones, receptors, antigens, drugs, antibodies and antigen binding fragments thereof, RNA, **DNA** and **oligonucleotides.**

USE - Presence or amount of analyte in sample can be determined by using photoprotein-binding reagent **conjugate** in binding assay (claimed).
Dwg.0/6

=>

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=> fil caplus
FILE 'CAPLUS' ENTERED AT 15:12:56 ON 26 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 26 Feb 2004  VOL 140 ISS 9
FILE LAST UPDATED: 25 Feb 2004  (20040225/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


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                  OR 185332-92-7 OR 92921-25-0
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                  106145-13-5 OR 92921-26-1
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L4   (        25) SEA FILE=REGISTRY ABB=ON  PLU=ON  PHENYL (L) ISOPROPYL (L)
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L8   (         7) SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 NOT L6
L9             8 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR 31252-85-4
L10          104 SEA FILE=CAPLUS ABB=ON  PLU=ON  SULFO (2W) (SMCC OR EMCS OR
                  GMBS OR KMUS OR MBS OR SIAB OR SMPB OR LC SMPT OR SVSB OR
                  SIACX OR SIA OR SIAXX OR NPIA)
L11          247 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 OR L10
L12       630930 SEA FILE=CAPLUS ABB=ON  PLU=ON  OLIGONUCLEOTIDE#/OBI OR
                  NUCLEOTIDE?/OBI OR DNA/OBI
L13      1270374 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEIN#/OBI
L14       135497 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 (L) L13
L15          693 SEA FILE=CAPLUS ABB=ON  PLU=ON  L14 (L) CONJUGAT?/OBI
L18            4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L15 AND L11
L19        53407 SEA FILE=CAPLUS ABB=ON  PLU=ON  (AMINO OR AMINE  OR NH2) (S)
                  (?NUCLEOTIDE? OR DNA)
L20         1037 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 (S) MODIF?
L21            6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND L15
L22          198 SEA FILE=CAPLUS ABB=ON  PLU=ON  L14 AND L20
L23            1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L22 AND L11
L24          114 SEA FILE=CAPLUS ABB=ON  PLU=ON  L19 AND L15
L25           15 SEA FILE=CAPLUS ABB=ON  PLU=ON  L24 AND (THIO# OR SULF?)
L26           23 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25 OR L23 OR L21 OR L18
L27           63 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND L12
L28           31 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND L13
L29           24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L28 AND ?LINK?
L30           13 SEA FILE=CAPLUS ABB=ON  PLU=ON  L29 AND CONJUG?
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L31 34 SEA FILE=CAPLUS ABB=ON PLU=ON L30 OR L26

=> d .ca l31 1-34

L31 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:836754 CAPLUS
DOCUMENT NUMBER: 139:341721
TITLE: Histone **conjugates** for delivery of drugs to cell nuclei
INVENTOR(S): Gilon, Chaim; Loyter, Abraham; Graessman, Adolf; Sperling, Joseph; Hariton-Gazal, Ilana
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Yeda Research and Development Co., Ltd.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086273	A2	20031023	WO 2003-IL279	20030403

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-370221P P 20020408
US 2002-429575P P 20021129

AB A **conjugate** of a histone moiety covalently attached to a macromol.-of-interest, in which the histone moiety is transportable through the cell membrane and importable into the cell nuclei, is disclosed. Further disclosed are chemical and recombinant methods of preparing such a **conjugate**, pharmaceutical compns. containing same and uses thereof for delivering therapeutically active macromols. into cells. A novel method for quant. determining a cytoplasmic uptake and/or a nuclear uptake of a moiety into cells is also disclosed.

IC ICM A61K
CC 63-5 (Pharmaceuticals)
ST cell nucleus drug delivery histone **conjugate**
IT Histones
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(H1, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)
IT Histones
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(H2A, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT Histones
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(H2B, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT Histones
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(H3, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT Histones
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(H4, **conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT Spheres
(beads; histone **conjugates** for delivery of drugs to cell nuclei)

IT Drug delivery systems
(carriers; histone **conjugates** for delivery of drugs to cell nuclei)

IT Enzymes, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(colorimetric reagents; histone **conjugates** for delivery of drugs to cell nuclei)

IT Histones
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT **DNA**
Gene, animal
Nucleic acids
Oligonucleotides
Proteins
RNA
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; histone **conjugates** for delivery of drugs to cell nuclei)

IT Animal tissue culture
Cell nucleus
Fluorescent substances
Linking agents
Microarray technology
Microtiter plates
Pigments, nonbiological
Sulfhydryl group
(histone **conjugates** for delivery of drugs to cell nuclei)

IT Glass, uses
RL: NUU (Other use, unclassified); USES (Uses)
(histone **conjugates** for delivery of drugs to cell nuclei)

IT Lymphocyte

(human; histone **conjugates** for delivery of drugs to cell nuclei)
IT Biological transport
(import; histone **conjugates** for delivery of drugs to cell nuclei)
IT Biological transport
(intracellular; histone **conjugates** for delivery of drugs to cell nuclei)
IT Human
(lymphocytes of; histone **conjugates** for delivery of drugs to cell nuclei)
IT Drug delivery systems
(targeted; histone **conjugates** for delivery of drugs to cell nuclei)
IT **103708-09-4**, **Sulfo-smcc**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** agent; histone **conjugates** for delivery of drugs to cell nuclei)
IT 58-85-5, Biotin
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(histone **conjugates** for delivery of drugs to cell nuclei)
IT 393511-86-9P 524943-98-4P
RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation)
(histone **conjugates** for delivery of drugs to cell nuclei)

L31 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:738727 CAPLUS
DOCUMENT NUMBER: 139:288452
TITLE: Electrogenerated chemiluminescence. 72. Determination of immobilized DNA and C-reactive protein on Au(111) electrodes using tris(2,2'-bipyridyl)ruthenium(II) labels
AUTHOR(S): Miao, Wujian; Bard, Allen J.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, TX, 78712-0165, USA
SOURCE: Analytical Chemistry (2003), 75(21), 5825-5834
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anodic electrogenerated chemiluminescence (ECL) with tri-n-propylamine (TPrA) as a coreactant was used to determine DNA and C-reactive protein (CRP) by immobilizations on Au(111) electrodes using tris(2,2'-bipyridyl)ruthenium(II) (Ru(bpy)32+) labels. A 23-mer synthetic single-stranded (ss) **DNA** derived from the Bacillus anthracis with an **amino-modified** group at the 5' end position was covalently attached to the Au(111) substrate precoated with a self-assembled **thiol** monolayer of 3-mercaptopropanoic acid (3-MPA) in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDAC) and then hybridized with a target ssDNA tagged with Ru(bpy)32+ ECL labels. Similarly, biotinylated anti-CRP species were immobilized effectively onto the Au(111) substrate precovered with a layer of avidin linked covalently via the reaction between avidin and a mixed **thiol** monolayer of 3-MPA and 16-mercaptohexadecanoic acid on Au(111) in the presence of EDAC and N-hydroxysuccinimide. CRP and anti-CRP tagged with Ru(bpy)32+ labels were then conjugated to the surface layer. ECL responses were generated from the modified electrodes described above by immersing them in a TPrA-containing electrolyte solution A series of electrode treatments, including blocking free -COOH groups with ethanol

amine, pinhole blocking with bovine serum albumin, washing with EDTA/NaCl/Tris buffer, and spraying with inert gases, were used to reduce the nonspecific adsorption of the labeled species. The ECL peak intensity was linearly proportional to the analyte CRP concentration over the range 1-24 μg/mL. CRP concns. of two unknown human plasma/serum specimens were measured by the standard addition method based on this technique.

CC 9-7 (Biochemical Methods)
Section cross-reference(s): 4, 10

IT Avidins
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(**conjugates**; electrogenerated chemiluminescence determination of immobilized **DNA** and C-reactive **protein** on Au(111) electrodes using tris(2,2'-bipyridyl)ruthenium(II) labels)

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:662897 CAPLUS
DOCUMENT NUMBER: 139:271618
TITLE: Affinity capture-facilitated preparation of aequorin-oligonucleotide conjugates for rapid hybridization assays
AUTHOR(S): Glynou, Kyriaki; Ioannou, Penelope C.; Christopoulos, Theodore K.
CORPORATE SOURCE: Department of Chemistry, University of Athens, Athens, 15771, Greece
SOURCE: Bioconjugate Chemistry (2003), 14(5), 1024-1029
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We report a general procedure for the preparation of biomol. conjugates that combine the mol. recognition properties of oligonucleotides with the high detectability of the photoprotein aequorin. Central to the conjugation protocols is the use of recombinant aequorin fused to a hexahistidine tag. In one protocol, an **amino-modified oligonucleotide** was treated with a homobifunctional cross-linker carrying two N-hydroxysuccinimide ester groups, and the derivative was allowed to react with (His)6-aequorin. A second strategy involved the introduction of protected **sulfhydryl** groups into (His)6-aequorin and subsequent reaction with a heterobifunctional linker containing a N-hydroxysuccinimide and a maleimide group. The strong, but reversible, binding of (His)6-aequorin to Ni2+-nitrilotriacetic acid agarose enabled the rapid and effective removal of the unreacted oligonucleotide, which otherwise diminishes the performance of the hybridization assay by competing with the conjugate for the complementary target sequence. Aequorin-oligo conjugates prepared by affinity capture showed similar performance with those purified by anion-exchange HPLC. The conjugates were applied to the development of rapid bioluminometric hybridization assays. The anal. range extended from 2 to 2000 pmol/L of target DNA. The reproducibility was less than 10%. The conjugate obtained from a reaction of 10 nmol of (His)6-aequorin is sufficient for about 5000 hybridization assays. The proposed conjugation strategy is general because a variety of reporter proteins can be fused to hexahistidine tag by using suitable vectors that are com. available.

CC 3-1 (Biochemical Genetics)

IT **Oligodeoxyribonucleotides**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**amino-modified** conjugates with aequorin; affinity capture-facilitated preparation of aequorin-**oligonucleotide**

conjugates for rapid hybridization assays)
IT Aequorins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fusion **protein** with hexahistidine tag, **conjugates** with oligodeoxyribonucleotides; affinity capture-facilitated preparation of aequorin-**oligonucleotide conjugates** for rapid hybridization assays)
IT 139-13-9D, Nitrilotriacetic acid, Ni2+-salt, immobilized on agarose
14701-22-5D, Ni2+, nitrilotriacetic acid-salt, biological studies
64134-30-1D, Hexahistidine, fusion **protein** with aequorin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(affinity capture-facilitated preparation of aequorin-**oligonucleotide conjugates** for rapid hybridization assays)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:639033 CAPLUS
DOCUMENT NUMBER: 139:193936
TITLE: Methods for preparation of DNA or protein microarrays and their use in diagnosis of disease
INVENTOR(S): Nassoy, Pierre; Potier, Marie Claude; Talini, Luc; Gibelin, Nathalie; Rossier, Jean
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique CNRS, Fr.; Institut Curie
SOURCE: Fr. Demande, 46 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2835829	A1	20030815	FR 2002-1791	20020213
WO 2003068712	A2	20030821	WO 2003-FR464	20030213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FR 2002-1791 A 20020213
AB The present invention relates to a method for preparation of a biochip which is activated for the covalent attachment of oligonucleotide or peptide probes on a solid support by a NHS-PEG-VS spacer. The invention also includes methods for detection of nucleic acids or peptides using biochips. The present invention also provides kits for detection, quant. or qual. anal. of nucleic acids or peptides in a sample, for purification of nucleic acids or peptides, for sequencing of nucleic acids, and for gene expression profiling or for the study and the detection of genetic polymorphisms for diagnosis of diseases.
IC ICM C07B051-00

ICS G01N033-543; C07K001-14; C12Q001-68
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 3, 14
IT **Amines**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(primary, deactivation of NHS on biochip using; methods for preparation of **DNA** or protein microarrays)
IT **Amino** group
Sulfhydryl group
(probe attached to biochip via; methods for preparation of **DNA** or protein microarrays)
IT Cyanine dyes
(probe **conjugate**, **sulfonated** derivative; methods for preparation of **DNA** or **protein** microarrays)
IT Nanocrystals
Nanoparticles
(probe **conjugate**; methods for preparation of **DNA** or **protein** microarrays)
IT 1760-24-3, N-(2-Aminoethyl)-3-**amino**-propyltrimethoxysilane
4420-74-0, (3-Mercaptopropyl trimethoxysilane 13598-78-2, Aminosilane
14044-97-4, Mercaptosilane
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(biochip support activated with; methods for preparation of **DNA** or protein microarrays)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:472604 CAPLUS
DOCUMENT NUMBER: 139:49507
TITLE: Synthesis and use of affinity probes directed toward adenine nucleotide-binding proteins
INVENTOR(S): Campbell, David A.; Wash, Paul
PATENT ASSIGNEE(S): Activx Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050248	A2	20030619	WO 2002-US39073	20021205
WO 2003050248	A3	20040122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003134303	A1	20030717	US 2002-213359	20020805

PRIORITY APPLN. INFO.: US 2001-339424P P 20011211

US 2002-213359 A 20020805

AB The invention relates to compns. and methods for the synthesis and use of adenosine nucleotide-binding protein-directed affinity labels. Adenosine nucleotide-binding proteins may be labeled with probes comprising adenosine, or an analog thereof, functionalized at the 5' position with reactive group capable of reacting with an amino acid side chain functionality at an adenosine nucleotide binding site, and at the 2' or 3' position with a tag for sequestering and/or identifying the resulting conjugate. In particular, one such probe is 5'-fluorosulfonylbenzoylamido-2'(3')-(2-TAMRA-amidoethylcarbamoyl)adenosine, shown to effectively label EGF receptor tyrosine kinase in A431 cells and insulin receptor kinase in boiled rat liver lysate. The probes may be used for determining the presence or amount of one or more adenosine nucleotide-binding proteins in a complex mixture, particularly a cellular mixture, for screening for drugs, and other purposes associated with the presence of the adenine nucleotide-binding protein(s) in a cell or changes in the presence, amount, activity, or relative concentration of the active adenosine nucleotide-binding protein.

IC ICM C12N

CC 9-15 (Biochemical Methods)

IT Functional groups
(acryl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide**-binding **proteins**)

IT Fluorescent substances
(adenosine **conjugates**; synthesis and use of affinity probes directed toward adenine **nucleotide**-binding **proteins**)

IT Functional groups
(chloroacetyl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide**-binding **proteins**)

IT Functional groups
(fluorosulfonyl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide**-binding **proteins**)

IT Functional groups
(vinylsulfonyl, in adenosine **conjugates** with fluorophores; synthesis and use of affinity probes directed toward adenine **nucleotide**-binding **proteins**)

IT 79-04-9, Chloroacetyl chloride 402-55-1, 4-Fluorosulfonylbenzoylchloride 530-62-1 814-68-6, Acryloyl chloride 14365-44-7 24424-99-5, Di-tert-butyl dicarbonate 51600-11-4 120718-52-7, TAMRA 146616-66-2, BODIPY-FL,SE **343934-41-8** 519054-52-5, Rhodamine green carboxylic acid succinimidyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and use of affinity probes directed toward adenine nucleotide-binding proteins)

L31 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:454606 CAPLUS
DOCUMENT NUMBER: 139:31760
TITLE: Methods and kits containing nanoparticle conjugated oligonucleotide probes for detection of nucleic acids using PCR
INVENTOR(S): Storhoff, James J.; Fritz, Brett M.; Herrmann, Mark
PATENT ASSIGNEE(S): Nanosphere, Inc., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003048769	A1	20030612	WO 2002-US38069	20021127

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003143604	A1	20030731	US 2002-306630	20021127

PRIORITY APPLN. INFO.: US 2001-334644P P 20011130

AB The present invention relates to the use of nanoparticle detection probes to monitor amplification reactions, especially polymerase chain reactions ('PCR'). More specifically, the present invention involves the use of nanoparticles oligonucleotide conjugates treated with a protective agent such as bovine serum albumin in an homogeneous assay format in order to quant. and qual. detect a target polynucleotide. A detectable change (preferably a color change) is brought about as a result of the hybridization of the oligonucleotides on the nanoparticles to the nucleic acid. The invention also provides compns. and kits comprising particles. The invention further provides methods of synthesizing unique nanoparticle-oligonucleotide conjugates, the conjugates. Finally, the invention provides a method of separating a selected nucleic acid from other nucleic acids. The preparation of colloidal gold nanoparticles from HAuCl4 is described. Particles show a color change upon aggregation. 3'-**Thiol** terminated oligonucleotides were immobilized on the surface of these particles. Oligonucleotide dependent aggregation and color changes were demonstrated and the hybridization conditions optimized.

IC ICM G01N033-53
ICS G01N033-00; G01N021-65; G01V005-00; G01J003-30; C12Q001-68; C07H019-00; C07H021-00; C07H021-02; C07H021-04

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9

IT Thiols (organic), biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(acid or **amine**-terminated, as protective agents for nanoparticle conjugated **oligonucleotide** probes; methods and kits containing nanoparticle conjugated **oligonucleotide** probes for detection of nucleic acids using PCR)

IT Albumins, biological studies
Antibodies
Caseins, biological studies
DNA
Organic compounds, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Proteins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as protective agents for nanoparticle **conjugated**

oligonucleotide probes; methods and kits containing nanoparticle **conjugated oligonucleotide** probes for detection of nucleic acids using PCR)

IT Peptides, biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**thiol**-containing, as linking agent for probe; methods and kits containing nanoparticle conjugated oligonucleotide probes for detection of nucleic acids using PCR)

IT 60-23-1, Mercaptoethylamine 71310-21-9, 11-Mercaptoundecanoic acid
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**thiol**-based linking agent; methods and kits containing nanoparticle conjugated oligonucleotide probes for detection of nucleic acids using PCR)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:335251 CAPLUS
DOCUMENT NUMBER: 138:334049
TITLE: Efficient synthesis of **protein-oligonucleotide conjugates**
INVENTOR(S): Farooqui, Firdous; Reddy, Parameswara M.
PATENT ASSIGNEE(S): Beckman-Coulter, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035830	A2	20030501	WO 2002-US32317	20021011
W: AU, CA, CN, DE, GB, JP				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
US 2003092901	A1	20030515	US 2001-32592	20011024

PRIORITY APPLN. INFO.: US 2001-32592 A 20011024

AB The present invention relates to an improved method for forming a protein-oligonucleotide conjugate. The method is particularly amenable for forming antibody-oligonucleotide conjugates. The invention further concerns the conjugate mols. produced using such improved methods.

IC ICM C12N
CC 9-14 (Biochemical Methods)
ST synthesis **protein oligonucleotide conjugate**
IT Antibodies
Oligonucleotides
Proteins
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(**conjugates**; efficient synthesis of **protein-oligonucleotide conjugates**)

IT **Conjugation** (molecular association)
Immunoassay
Nucleic acid hybridization
(efficient synthesis of **protein-oligonucleotide conjugates**)

IT Avidins

Biliproteins
Enzymes, analysis
Immunoglobulins
RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 4781-83-3, Traut's reagent
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 9001-78-9, Alkaline phosphatase 9002-13-5, Urease 9013-20-1, Streptavidin 9031-11-2, β-Galactosidase
RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
(efficient synthesis of **protein-oligonucleotide conjugates**)

IT **103708-09-4, Sulfo-SMCC**
RL: RCT (Reactant); RACT (Reactant or reagent)
(efficient synthesis of **protein-oligonucleotide conjugates**)

IT 9003-99-0, Peroxidase
RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
(horseradish; efficient synthesis of **protein-oligonucleotide conjugates**)

L31 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173820 CAPLUS
DOCUMENT NUMBER: 138:182042
TITLE: Methods for haplotyping analysis by detection of single nucleotide polymorphisms
INVENTOR(S): Fenger, Mogens; Bentzen, Joan
PATENT ASSIGNEE(S): Hvidovre Hospital, Den.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018835	A2	20030306	WO 2002-DK552	20020822

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2001-1252 A 20010823
AB The present invention describes a method and kits for determining the genetic

haplotype (linkage phase) of a part of an individual genotype, by determining the presence or absence of two or more specific nucleotide polymorphisms on one of a pair of homologous chromosomes. Amplification of nucleic acids may be performed by PCR, Ligase Chain Reaction, Nucleic-Acid Sequence-Based Amplification, strand displacement amplification, rolling circle amplification, T7-polymerase amplification.

IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9
IT **Proteins**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(A, **oligonucleotide** probe **conjugate**; methods for haplotyping anal. by detection of single **nucleotide** polymorphisms)
IT Immunoglobulins
Proteins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(G, **oligonucleotide** probe **conjugate**; methods for haplotyping anal. by detection of single **nucleotide** polymorphisms)
IT **Sulfhydryl** group
(nucleic acid conjugate; methods for haplotyping anal. by detection of single nucleotide polymorphisms)
IT **Amines**, biological studies
Phosphates, biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primary, nucleic acid conjugate; methods for haplotyping anal. by detection of single **nucleotide** polymorphisms)

L31 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:160521 CAPLUS
DOCUMENT NUMBER: 138:216548
TITLE: DNA and protein sequences of Rhodococcus erythropolis cystathionine β-synthase sequence homolog and the uses of the protein for repression of the expression of the genes for desulfurization
INVENTOR(S): Kurane, Ryuichiro; Tanaka, Yasuhiro; Marubashi, Kenji
PATENT ASSIGNEE(S): National Institute of Advanced Industrial Science and Technology, Japan; Kokusai Sekiyu Koryu Center
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003061669	A2	20030304	JP 2001-254269	20010824

PRIORITY APPLN. INFO.: JP 2001-254269 20010824
AB The invention provides DNA and protein sequences for a gene from Rhodococcus erythropolis sharing sequence homol. with Streptomyces venezuela cystathionine β-synthase. The gene was identified by randomly knocking out the genes associated with desulfurization in thiophene degradable microorganism. The gene can be used for producing of **sulfate** ion independent desulfurization microorganism.
IC ICM C12N015-09

ICS C12N001-20; C12N001-21; C12R001-01; C12R001-32; C12R001-125; C12R001-10; C12R001-06; C12R001-19; C12R001-40; C12R001-385; C12R001-39
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 10
IT 91-20-3D, Naphthalene, thiophene **conjugates** 95-15-8, Benzothiophene 110-02-1D, Thiophene, naphthyl derivs. 110-82-7D, Cyclohexane, dibenzothiphene **conjugates** 132-65-0, Dibenzo thiophene 132-65-0D, Dibenzothiophene, cyclohexyl derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**DNA** and **protein** sequences of Rhodococcus erythropolis cystathionine β-synthase sequence homolog and the uses of the **protein** for repression of the expression of the genes for desulfurization)
IT 500686-67-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**amino** acid sequence; **DNA** and protein sequences of Rhodococcus erythropolis cystathionine β-synthase sequence homolog and the uses of the protein for repression of the expression of the genes for desulfurization)

L31 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:937303 CAPLUS
DOCUMENT NUMBER: 138:20443
TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Bio Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002355079	A2	20021210	JP 2002-69354	20020313

PRIORITY APPLN. INFO.: JP 2001-73183 A 20010314
JP 2001-74993 A 20010315
JP 2001-102519 A 20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.
IC ICM C12N015-09
ICS C12N015-09; C12Q001-02; C12Q001-68; G01N033-53; G01N037-00
CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 2, 4, 5, 9, 13

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (E74-like **factor** 1 (ets domain transcription factor); endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HMG-box containing protein 1; endocrine disruptor screening using **DNA** chips of endocrine disruptor-responsive genes)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HSPC015; endocrine disruptor screening using **DNA chips** of endocrine disruptor-responsive genes)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**KIAA0033**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PNO099 son3 **protein**; **endocrine** disruptor **screening** using **DNA** chips of endocrine disruptor-**responsive** genes)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (PTH-responsive osteosarcoma **B1 protein**; **endocrine** disruptor screening using **DNA** chips of endocrine disruptor-responsive genes)

IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (chondroitin **sulfate**-containing; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (muscle-blind, sequence **homolog**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (myelocytomatosis oncogene; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (myeloid differentiation primary **response** gene (88); endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT Nicotinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (nicotinic cholinergic **receptor**, β **polypeptide** 1 (muscle); endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT **Transport** proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**nucleoside transporter**, equilibrative **nitrobenzyl**-thioinosine sensitive nucleoside transporter **ENTI**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (protein tyrosine phosphatase receptor type f polypeptide (PTPRF) interacting protein (liprin) α1; endocrine disruptor screening

using DNA chips of endocrine disruptor-responsive genes)

IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (retinol binding protein, CRBP (cellular **retinol** binding protein), cellular retinol binding protein 2; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study) (small inducible **cytokine** A27, A9, A5; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (synuclein γ ; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT 37278-34-5, Heparitin N-deacetylase/N-**sulfotransferase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (-N-deactylase; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT 9023-09-0, **Sulfotransferase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (2B member 1; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT 9023-05-6, **Sulfurtransferase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (3 MERCA-pitopyruvate **sulfurtransferase**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT 73361-25-8, Heparitin N-deacetylase/N-**sulfotransferase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (N-**sulfotransferase**; endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes)

IT 110463-31-5, **Amine** N-**sulfotransferase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**amine** N-**sulfotransferase**; endocrine disruptor screening using **DNA** chips of endocrine disruptor-responsive genes)

IT 1393-25-5, Secretin 9000-94-6, Antithrombin-III 9001-05-2, Catalase 9001-16-5, Cytochrome c oxidase 9001-40-5, Glucose-6 phosphate dehydrogenase 9001-42-7, α-Glucosidase 9001-45-0, Glucuronidase β 9001-48-3, Glutathione reductase 9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase 9001-61-0, Cytosolic aminopeptidase 9001-63-2, Lysozyme 9001-64-3, Malate dehydrogenase 9001-91-6, Plasminogen 9002-03-3, Dihydrofolate reductase 9002-62-4, Prolactin, biological studies 9004-02-8, Lipoprotein lipase 9012-37-7, Aminoacylase-1 9012-93-5, Ferrochelatase 9013-10-9, Glucosamine-6-phosphate isomerase 9013-93-8, Phospholipase 9014-18-0, Nicotinamide nucleotide transhydrogenase 9023-44-3, Tryptophanyl-tRNA synthetase 9023-48-7, Seryl-tRNA synthetase 9023-56-7, CTP synthase 9023-58-9, Argininosuccinate synthetase 9023-69-2, Asparagine synthetase 9023-88-5 9023-90-9, Methylmalonyl-CoA mutase 9024-20-8, Ribulose phosphate 3 epimerase 9024-60-6, Ornithine decarboxylase 9024-70-8, Uroporphyrinogen decarboxylase 9025-15-4, Biotinidase 9025-73-4, Phosphoserine phosphatase 9026-00-0, Lysosomal acid lipase 9026-23-7, Carbamoyl-phosphate synthase 9026-24-8, Thiamin pyrophosphokinase 9026-30-6, Poly (A) polymerase 9026-67-9, Choline kinase 9027-13-8, Enoyl-CoA hydratase 9027-32-1, Aspartyl-tRNA synthetase 9027-44-5, Hydroxymethylglutaryl-CoA synthase 9027-67-2, Terminal deoxynucleotidyl transferase 9027-80-9, Adenine phosphoribosyl transferase 9027-81-0, Adenylosuccinate Lyase 9028-21-1, Sorbitol dehydrogenase 9028-40-4, 3-Hydroxyacyl-CoA dehydrogenase 9028-61-9, Estradiol 17β-dehydrogenase 9029-17-8, Pyrroline-5-carboxylate reductase

9029-38-3, **Sulfite** oxidase 9030-22-2, Uridine phosphorylase 9030-23-3, Thymidine phosphorylase 9030-24-4, Uracil phosphoribosyltransferase 9030-38-0 9030-53-9, Galactokinase 9030-83-5, 3-Hydroxy-3-methylglutaryl-CoA lyase 9031-19-0, Saccharopine dehydrogenase 9031-37-2, Ceruloplasmin 9031-71-4, Alanyl-tRNA synthetase 9031-82-7, Amidophosphoribosyltransferase 9031-86-1, Aspartoacylase 9032-03-5, Phosphoribosylaminoimidazolecarboxamide formyltransferase 9032-25-1, NADH cytochrome B5 reductase 9032-59-1, Fumarylacetoacetate hydrolase 9032-71-7, 2,3-Oxidosqualene-lanosterol cyclase 9032-73-9, Neuropathy target esterase 9032-88-6, Fumarate hydratase 9033-27-6, Isopentenyl-diphosphate δ isomerase 9035-39-6, Cytochrome b5 9035-42-1, Cytochrome c1 9037-62-1, Glycyl-tRNA synthetase 9037-65-4, α-L-Fucosidase 9040-59-9, Phosphodiesterase 1 9042-64-2, DOPA decarboxylase 9045-77-6, Fatty acid synthase 9047-22-7, Cathepsin B 9054-54-0, Transacylase 9054-84-6, Xanthine dehydrogenase 9059-11-4, **Amine** oxidase 9059-48-7, Sepiapterin reductase 9067-83-8, Phosphatidate cytidylyltransferase 9068-16-0, Poly(ADP ribose) glycohydrolase 9068-41-1, Carnitine palmitoyltransferase 9074-91-3, Hydroxymethylbilane synthase 9075-29-0, 3 Phosphoglycerate dehydrogenase 9075-78-9, Ethanolamine kinase 9075-81-4, β-Galactoside α-2,6-sialyltransferase 9076-57-7, Histone deacetylase 9076-84-0, Coproporphyrinogen oxidase 12651-28-4, Transcobalamin 2 37184-63-7, Myoinositol 1-monophosphatase 37205-49-5, Methylmalonate-semialdehyde dehydrogenase 37211-69-1, 2,3-Bisphosphoglycerate mutase 37237-43-7, Galactosyltransferase β-1,4-GalT V 37255-37-1, E.C. 1.3.3.2 37255-38-2, Glutaryl-CoA dehydrogenase 37259-54-4, DTDP-glucose 4,6-dehydratase 37274-61-6, Isovaleryl-CoA dehydrogenase 37277-82-0, Spermidine synthase 37341-57-4, Succinate:CoA ligase 39471-28-8, Deoxyguanosine kinase 51110-01-1, Somatostatin 52660-18-1, Casein kinase 1 55354-43-3, Arylsulfatase B 59088-23-2, Dihydroorotate dehydrogenase 59298-90-7, UDP-galactose:glucosylceramide β1,4-galactosyltransferase 60320-99-2, N-Acetylglucosamine-6-**sulfatase** 65997-74-2, Cathepsin F 67339-00-8, α2,8-Sialyltransferase 67763-97-7, Insulin-like growth factor 2 79079-11-1, Calpastatin 80295-40-5, Complement C2 80295-48-3, Complement C4 80295-62-1, Complement factor B 80295-65-4, Complement factor H 81181-72-8, γ-Glutamyl carboxylase 81611-75-8, Fructose-2,6-bisphosphatase 82062-90-6, NAD-dependent methylenetetrahydrofolate dehydrogenase 82391-38-6, Branched chain keto acid dehydrogenase kinase 82707-54-8, Neprilysin 83268-44-4 86480-67-3, Ubiquitin carboxyl-terminal hydrolase 87683-70-3, Pterin-4α-carbinolamine dehydratase 90698-32-1, Leukotriene C4 synthase 101149-94-4, Tripeptidyl peptidase II 102577-19-5, Neuromedin B 109136-49-4, Ubiquitin-specific protease 122320-05-2, Secretory leukocyte protease inhibitor 124861-55-8 137632-08-7, Mitogen activated protein kinase 1 141349-86-2, Cyclin-dependent kinase 2 141467-21-2, Calcium/calmodulin-dependent protein kinase I 142243-03-6, Plasminogen activator inhibitor type II 142539-77-3, Mast cell protease 5 142805-56-9, DNA topoisomerase II 143180-75-0, DNA topoisomerase I 144114-16-9, Focal adhesion kinase 144697-17-6, c-Src tyrosine kinase 145809-21-8, Tissue inhibitor of metalloproteinase 3 146480-35-5, Matrix metalloproteinase 2 146480-49-1, MMCP-6 protease 146838-30-4, Mitogen-activated protein kinase-activated protein kinase 2 147014-97-9, Cyclin dependent kinase 4 149316-81-4, 2-Hydroxyphytanoyl-CoA lyase 149371-24-4, Neurolysin 150605-50-8, Neuronal tyrosine/threonine phosphatase 1 152478-57-4, Janus kinase 2 153190-47-7, Gene PTK2 tyrosine kinase 165245-94-3, NimA-related kinase 2 165245-99-8, Polo-like kinase 167397-96-8, Interleukin-1 receptor-associated kinase 169277-44-5, Sphingosine-1-phosphate phosphatase 169592-62-5,

Cyclin-dependent kinase 10 170780-57-1, LIM kinase 172306-41-1, Protein kinase PCTAIRE-1 172399-47-2, BOMAPIN 173585-04-1, Integrin-linked kinase 176023-64-6, Mitogen-activated protein kinase 12 178037-70-2, Serum and glucocorticoid regulated protein kinase 180189-96-2, Caspase 9 182372-15-2, Caspase 6 184049-62-5, Gene DUSP6 MAP kinase phosphatase 187247-72-9, Endonuclease G 188417-84-7, Vascular endothelial growth factor C 191359-13-4, MAP kinase-interacting kinase 1 192230-91-4, Mitogen-activated protein kinase kinase 4 194739-73-6, Mitogen-activated protein kinase kinase 6 196717-99-4, Prenylcysteine lyase 206566-35-0, Molybdopterin synthase **sulfurylase** 212625-17-7, SPAK protein kinase 214210-47-6, Neuropilin 1 216503-96-7, Caspase 11 223610-95-5, Matrix metalloproteinase MMP-23 230951-53-8, Caspase 12 252852-50-9, SUMO-1 conjugate proteinase 252901-98-7, Tousled-like kinase 1 258336-77-5, UNC51.2 serine/threonine kinase 288307-53-9, Inositol 1,3,4-trisphosphate 5/6 kinase 292850-69-2, Nardilysin 306298-47-5, MAP kinase phosphatase-1 321976-25-4, Sialyltransferase 324751-96-4, Stanniocalcin 2 324752-01-4, Stanniocalcin 1 327046-95-7, Mitogen activated protein kinase kinase 5 335135-28-9, Cytochrome P450 2D10 338969-69-0, Cytochrome P450 2F2 353498-78-9, Mitogen activated protein kinase 6 362516-16-3, Conserved helix-loop-helix ubiquitous kinase 374936-45-5, Cytochrome P450 2C40 409105-92-6, Microtubule-associated testis-specific serine/threonine protein kinase 440356-82-1, Cytochrome P450 7B1 443906-18-1, Receptor protein tyrosine phosphatase K 464896-43-3, Transmembrane serine proteinase 475489-73-7, Calcium/calmodulin-dependent protein kinase II 478187-31-4, P 450 2J6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endocrine disruptor screening using **DNA** chips of endocrine disruptor-responsive genes)

L31 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:734843 CAPLUS
DOCUMENT NUMBER: 138:68558
TITLE: Site-specific DNA cleavage of synthetic NarL sites by an engineered Escherichia coli NarL protein-1,10-phenanthroline cleaving agent
AUTHOR(S): Xiao, Gaoping; Cole, Daniel L.; Gunsalus, Robert P.; Sigman, David S.; Chen, Chi-Hong B.
CORPORATE SOURCE: Department of Microbiology, Immunology, University of California, Los Angeles, CA, 90095-1489, USA
SOURCE: Protein Science (2002), 11(10), 2427-2436
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The NarL response regulatory protein of Escherichia coli has been engineered by covalent modification with 1,10-phenanthroline (OP) to create a set of site-specific DNA-cleaving agents. This was accomplished by introducing single cysteine **amino** acid replacements at selected locations within the C-terminal **DNA**-binding domain in or nearby the helix 8 to helix 9 region of the NarL protein using site-directed mutagenesis. Of 18 modified NarL-OP proteins made, 13 retained the ability to bind DNA as evidenced by gel mobility assays, whereas 10 of the 1,10-phenanthroline-modified proteins also exhibited specific cleavage activity for a synthetic NarL recognition sequence. These DNA-cleaving agents were divided into two groups based on the location of the cleavage sites. The first class set cleaved the DNA nearby the center of a synthetic 7-2-7 sequence composed of two NarL heptamer sites separated by a 2-bp spacer element. The second class cut the DNA at the periphery of the 7-2-7 sequence. The cleavage data are

consistent with the ability of two NarL monomers to recognize and bind to the DNA in a head-to-head orientation. A second set of DNA-cleaving agents was constructed using the C-terminal domain of NarL called NarLC. Similar cleavage patterns were observed whether full-length NarL or NarLC was used. The availability of 1,10-phenanthroline-modified NarL and NarLC proteins opens up the possibility to explore the position, orientation, and number of NarL recognition sites at E. coli promoters predicted to contain multiple and complex arrangements of NarL-binding sites.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 9

IT 52-90-4D, L-Cysteine, **conjugates** with orthophenanthroline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(residues 162, 174, 181, 201, 204 or 211 of NarL; site-specific **DNA** cleavage of synthetic NarL sites by an engineered Escherichia coli NarL **protein**-1,10-phenanthroline cleaving agent)

IT 111047-29-1D, **conjugates** with NarL **proteins**
182685-66-1D, **conjugates** with NarL **proteins**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(site-specific **DNA** cleavage of synthetic NarL sites by an engineered Escherichia coli NarL **protein**-1,10-phenanthroline cleaving agent)

IT 107-96-0, 3-Mercaptopropionic acid 7722-84-1, Hydrogen peroxide, reactions 7758-98-7, Copper **sulfate**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(site-specific DNA cleavage of synthetic NarL sites by an engineered Escherichia coli NarL protein-1,10-phenanthroline cleaving agent)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:367208 CAPLUS
DOCUMENT NUMBER: 136:366115
TITLE: Ligand-aminodextran-marker **conjugates** and uses thereof
INVENTOR(S): Siiman, Olavi; Burshteyn, Alexander; Mylvaganam, Ravindra; Raynor, Robert; Roth, Patricia; Smith, Cecilia; Wilkinson, Julie
PATENT ASSIGNEE(S): Coulter International Corp., USA
SOURCE: U.S., 58 pp., Cont.-in-part of U.S. 5,994,089.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387622	B1	20020514	US 1999-403919	19991027
US 5891741	A	19990406	US 1997-857941	19970516
US 5994089	A	19991130	US 1997-976031	19971121
WO 9852040	A1	19981119	WO 1998-US9774	19980514

W: JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1997-857941 A2 19970516
US 1997-976031 A2 19971121
WO 1998-US9774 W 19980514

AB Ligand-aminodextran-(phycobiliprotein or tandem dye) **conjugates**

useful for detection of a desired target biol. material by providing an enhanced fluorescent signal are described. Also described is a method for a single-measurement quantification of multiple populations of cells based upon the labeling of different pairs of cell populations, each pair containing mutually exclusive cell receptors which are expressed at substantially similar receptor densities with labeled ligands for each receptor. One cell population is labeled with a ligand capable of binding to a first cell surface receptor which ligand is directly **conjugated** to a fluorescent phycobiliprotein or tandem dye; and a second cell population is labeled with a ligand capable of binding to a second cell surface receptor, which ligand is cross-**linked** to an aminodextran which is **conjugated** to a fluorescent phycobiliprotein or tandem dye. Monoclonal antibody-phycoerythrin **conjugates** and monoclonal antibody-aminodextran-phycoerythrin **conjugates** were prepared and used in flow cytometric anal. of whole blood.

IC ICM G01N033-68
NCL 435006000
CC 9-4 (Biochemical Methods)
Section cross-reference(s): 15
ST ligand aminodextran marker **conjugate** flow cytometry; fluorescent phycobiliprotein ligand aminodextran flow cytometry; monoclonal antibody aminodextran phycoerythrin **conjugate** blood analysis
IT Cyanine dyes
(5.1, **conjugates** with phycoerythrin and with ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Allophycocyanins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(B, **conjugates** with ligands; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Immunoglobulins
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(G1, monoclonal; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Immunoglobulins
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(M, monoclonal; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Histocompatibility antigens
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(MHC (major histocompatibility complex), complexes with peptide and streptavidin or avidin, as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Peptides, preparation
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(MHC complexes and complexes with streptavidin or avidin, as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Phycoerythrins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(R-phycoerythrins, **conjugates** with ligands; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Biological materials
(anal. of; ligand-aminodextran-marker **conjugates** and uses thereof)
IT CD19 (antigen)
CD3 (antigen)

CD45RO (antigen)
CD56 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to; ligand-aminodextran-marker **conjugates** and uses thereof)

IT **Proteins**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(blue fluorescent, as label; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Avidins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(complexes with MHC-peptide, as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Ligands
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugated**; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Allophycocyanins
Biliproteins
Phycocyanins
Phycoerythrins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates** with ligands; ligand-aminodextran-marker **conjugates** and uses thereof)

IT **Oligonucleotides**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Antibodies
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(**conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Cytometry
(flow; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Immunoglobulins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fragments, **conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)

IT **Proteins**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(green fluorescent, as label; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Interleukin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 12, β chain, monoclonal antibody to human; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Interleukin 12
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(ligand as antibody to; ligand-aminodextran-marker **conjugates** and uses thereof)

IT Blood analysis
Fluorescence
Human
Leukocyte
T cell (lymphocyte)
(ligand-aminodextran-marker **conjugates** and uses thereof)

IT Nucleic acids
RL: ANT (Analyte); ANST (Analytical study)
(ligand-aminodextran-marker **conjugates** and uses thereof)
IT Receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(ligands binding to; ligand-aminodextran-marker **conjugates** and uses thereof)
IT CD8 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal antibody to; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Antibodies
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(monoclonal, **conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Antibodies
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(monoclonal; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Lymphocyte
(natural killer cell, monoclonal antibody to human; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Molecular weight
(of antibody-aminodextran-phycobiliprotein **conjugates**; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Dyes
(phycobiliprotein-containing tandem, **conjugates** with ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
IT Cell
(single-measurement quantification of multiple populations of; ligand-aminodextran-marker **conjugates** and uses thereof)
IT 9004-54-0, Dextran, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(T-2M; ligand-aminodextran-marker **conjugates** and uses thereof)
IT 109-76-2, 1,3-Diaminopropane
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(aminodextran substituted with; ligand-aminodextran-marker **conjugates** and uses thereof)
IT 9013-20-1DP, Streptavidin, complexes with MHC-peptide
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(as ligand; ligand-aminodextran-marker **conjugates** and uses thereof)
IT 27072-45-3D, FITC, **conjugates** with antibody to CD45RO
82354-19-6D, Texas Red, **conjugates** with phycoerythrin and with ligand
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(ligand-aminodextran-marker **conjugates** and uses thereof)
IT 37293-51-9DP, Aminodextran, **conjugates** with phycobiliprotein or tandem dye and **crosslinked** with ligand 88475-75-6DP, ECD, **conjugates** with aminodextran and ligand 146368-14-1DP, Cy5, **conjugates** with allophycocyanin and with ligand 169799-14-8DP, Cy7, **conjugates** with phycoerythrin or allophycocyanin and with ligand
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST

(Analytical study); PREP (Preparation); USES (Uses)
(ligand-aminodextran-marker **conjugates** and uses thereof)
IT 37293-51-9, Aminodextran
RL: RCT (Reactant); RACT (Reactant or reagent)
(ligand-aminodextran-marker **conjugates** and uses thereof)
IT 6539-14-6, 2-Iminothiolane
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with R-phycoerythrin or monoclonal antibody;
ligand-aminodextran-marker **conjugates** and uses thereof)
IT **103708-09-4, Sulfo-SMCC**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with monoclonal antibodies or aminodextran;
ligand-aminodextran-marker **conjugates** and uses thereof)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:265431 CAPLUS
DOCUMENT NUMBER: 134:291071
TITLE: High affinity RNase H-recruiting oligonucleotides containing bicyclic nucleoside analogs
INVENTOR(S): Wahlestedt, Claes; Jakobsen, Mogens Havsteen
PATENT ASSIGNEE(S): Exiqon A/S, Den.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025248	A2	20010412	WO 2000-DK550	20001003
WO 2001025248	A3	20010830		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1224280	A2	20020724	EP 2000-962273	20001003
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511016	T2	20030325	JP 2001-528192	20001003

PRIORITY APPLN. INFO.:
DK 1999-1422 A 19991004
US 1999-157724P P 19991005
WO 2000-DK550 W 20001003

AB The present invention relates to the field of bicyclic DNA analogs, e.g., LNA and LNA modifications, which are useful for designing oligomers that form high affinity duplexes with complementary RNA wherein said duplexes are substrates for RNase H. The oligonucleotides may be partially or fully composed of LNA analogs with very high affinity and ability to recruit RNase H. The implications are that oxy-LNA by itself may be used to construct novel antisense mols. with enhanced biol. activity. Alternatively, oxy-LNA may be used in combination with non-oxy-LNA, such as standard **DNA**, RNA or other analogs, e.g. **thio**-LNA or

amino-LNA, to create high affinity, RNase H recruiting anti-sense compds. without the need to adhere to any fixed design.
IC ICM C07H021-00
CC 3-1 (Biochemical Genetics)
IT Antibodies
Enzymes, biological studies
Haptens
Peptides, biological studies
Polysaccharides, biological studies
Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**conjugates** with locked nucleic acids; high affinity RNase H-recruiting **oligonucleotides** containing bicyclic nucleoside analogs)

L31 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:457085 CAPLUS
DOCUMENT NUMBER: 133:85091
TITLE: Targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors
INVENTOR(S): Boucher, Richard C., Jr.; Pickles, Raymond J.; Rideout, Janet L.; Pendergast, William; Yerxa, Benjamin R.; Douglass, James G., III
PATENT ASSIGNEE(S): The University of North Carolina At Chapel Hill, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039145	A1	20000706	WO 1999-US30658	19991222
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140967	A1	20011010	EP 1999-966577	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-219672 A 19981223
US 1998-219698 A 19981223
WO 1999-US30658 W 19991222
OTHER SOURCE(S): MARPAT 133:85091
AB A method of delivering foreign nucleic acid (e.g., a gene) into a cell by attaching a virus containing the nucleic acid to a G protein coupled receptor (i.e., a seven transmembrane receptor such as the P2Y2 receptor) that is internalized upon ligand binding. The virus may be attached to the receptor by means of a bridging antibody, or by binding an antibody specific for the receptor with an antibody specific for the virus, wherein the antibody that specifically binds with the receptor and the antibody that specifically binds to the virus are cross-**linked**. Alternatively, the virus may express a peptide that specifically binds to

the receptor. The receptor may be induced to internalize by means of the addition of a ligand known to trigger internalization of the receptor into the cell. Purinoceptors. specifically the P2Y2 receptor, were identified on the surface of the apical surface of the airway epithelium. Cells presenting the P2Y2 receptor containing a hemagglutinin epitope were incubated with adenovirus carrying a lacZ reporter gene and labeled with a bispecific antibody to the epitope and the knob protein of adenovirus. The virus was rapidly internalized upon exposing the cells to ATPγS.

IC ICM C07H021-00
ICS C07H021-02; A61K009-12; A61K031-70

CC 3-1 (Biochemical Genetics)

ST G **protein** coupled receptor vector internalization; endocytosis transforming **DNA** G **protein** coupled receptor

IT Bradykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(B2; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Purinoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(P2U; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Adeno-associated virus
Herpesviridae
Human adenovirus
Lentivirus
Murine leukemia virus
Retroviral vectors
(as gene transfer vector; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**conjugates**, in binding of virus vectors to G **protein** -coupled receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT **Oligonucleotides**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(dinucleotides, in stimulation of uptake of viral vectors bound to G **protein**-couple receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Respiratory tract
(epithelium, transformation of cells of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Hemagglutinins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(epitope of, in targetting of viral gene transfer vectors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Cystic fibrosis
(gene therapy of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in binding of virus vectors to G **protein**-coupled receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Catecholamines, biological studies
Nucleosides, biological studies
Nucleotides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(in stimulation of uptake of viral vectors bound to G **protein** -couple receptors; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Biological transport
(internalization, receptor-mediated; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Endocytosis
(receptor-mediated; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Gene therapy
(targeted gene delivery in; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Transformation, genetic
Virus vectors
(targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT G **protein**-coupled receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(αvβ3, in internalization of adenovirus; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(αvβ5, in internalization of adenovirus; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT Adrenoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(β2; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)
IT 58-82-2P, Bradykinin 80295-54-1P, Complement C5a
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(in stimulation of uptake of viral vectors bound to G **protein** -couple receptors; targeted gene transfer and internalization of virus

vectors using G **protein** coupled receptors)

IT 280549-85-1P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and reactions of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 280549-82-8P 280549-83-9P 280549-84-0P 280549-87-3P, 2-Bromo-4'-[(6-bromohexanoyl)amino]acetophenone 280549-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 280549-76-0P 280549-78-2P 280549-80-6P 280549-91-9P 280549-92-0P 280549-94-2P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and uses of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 58-97-9, Uridine 5'-monophosphate, reactions 99-92-3, 4'-Aminoacetophenone 530-62-1 22809-37-6, 6-Bromohexanoyl chloride 72040-63-2, Succinimidyl-6-(biotinamido) hexanoate 93285-75-7, N-Iodoacetyl-N'-biotinylhexylenediamine 109276-34-8 280549-77-1 280549-79-3 280549-81-7 280549-86-2 280549-88-4, 4'-[(6-Bromohexanoyl)amino]acetophenone 280549-90-8 280549-93-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactions of; targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

IT 60-23-1, Mercaptoethylamine **92921-25-0**, **Sulfo-MBS 185332-92-7**, **Sulfo-GMBS**
RL: RCT (Reactant); RACT (Reactant or reagent)
(targeted gene transfer and internalization of virus vectors using G **protein** coupled receptors)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:254039 CAPLUS
DOCUMENT NUMBER: 132:289590
TITLE: Peptide-enhanced cationic lipid transfections
INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.; Gebeyehu, Gulilat
PATENT ASSIGNEE(S): Life Technologies, Inc., USA
SOURCE: U.S., 103 pp., Cont.-in-part of U.S. 5,736,392.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6051429	A	20000418	US 1997-818200	19970314
US 5736392	A	19980407	US 1996-658130	19960604
WO 9840502	A1	19980917	WO 1998-US5232	19980316

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
GA, GN, ML, MR, NE, SN, TD, TG

AU 9865622	A1	19980929	AU 1998-65622	19980316
EP 1007699	A1	20000614	EP 1998-911737	19980316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517939	T2	20011009	JP 1998-539899	19980316
US 6376248	B1	20020423	US 1998-39780	19980316
US 2003144230	A1	20030731	US 2002-200879	20020723

PRIORITY APPLN. INFO.:

US 1995-477354	B2	19950607
US 1996-658130	A2	19960604
US 1997-818200	A	19970314
US 1998-39780	A1	19980316
WO 1998-US5232	W	19980316
US 2001-911569	A1	20010723

AB The present invention provides compns. useful for transfecting eukaryotic cells comprising nucleic acid complexes with peptides, wherein the peptide is optionally covalently coupled to a nucleic acid-binding group, and cationic lipids or dendrimers as transfection agents. The invention also provides transfection compns. in which a peptide is covalently **linked** to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection compns. or covalent attachment of peptides to transfection agents results in enhanced transfection efficiency. Methods for the preparation of transfection compns. and methods of using these transfection compns. as intracellular delivery agents and extracellular targeting agents are also disclosed.

IC ICM C12N015-64
ICS C12N015-63; C12N007-00; C12N015-11

NCL 435458000

CC 3-2 (Biochemical Genetics)

ST peptide polycation **DNA** complex transformation efficiency; polyamine peptide **DNA** complex transformation efficiency; spermine peptide **DNA** complex transformation efficiency

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(BPI (bactericidal/permeability-increasing), increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(E5, peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NLS (nuclear location signal sequence)-containing, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Lipids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cationic, in transformation; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **DNA**

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(complexes, **conjugates**; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusogenic, increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hexon, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Cell adhesion molecules
Fibronectins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT RGD peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Transformation, genetic
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Hemagglutinins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(influenza virus, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nucleic acid-binding, peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Alphavirus
Influenza virus
Vesicular stomatitis virus
(peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Amines, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamines, nonpolymeric, complexes with **DNA**; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Animal cell
Fibroblast

(transformation of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Dendritic polymers
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Glycoproteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(viral, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **92921-26-1**, **Sulfo-SMPB**
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation spermine-containing peptides; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT 213131-54-5P 213131-55-6P 213131-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation spermine-containing peptides; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT 213131-57-8 213131-71-6 213131-72-7 213131-74-9 213131-76-1 213131-78-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT 71-44-3D, Spermine, peptide **conjugates**, complexes with nucleic acids 87695-40-7 95214-35-0 117138-20-2 127258-63-3 250252-75-6 264129-76-2 264129-83-1 264130-22-5 264130-52-1 264134-53-4 264134-54-5 264134-55-6 264134-56-7 264134-57-8 264134-58-9 264227-38-5
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT 2462-63-7, Lipofectace 104162-48-3, DOTMA 124050-77-7, DOGS 144189-73-1, DOTAP 158571-62-1, Lipofectamine 163442-69-1D, Starburst 6th generation, **conjugates** with lysine or arginine 163442-70-4D, Starburst 7th generation, **conjugates** with lysine or arginine 163442-72-6D, Starburst 9th generation, **conjugates** with lysine or arginine 168479-03-6, DOSPA 178532-92-8, DOSPER 189203-05-2, DMRIE-C 213131-59-0 213131-62-5 213131-65-8 213131-68-1 213131-69-2 213186-72-2, DMRIE-DOPE mixture 213252-20-1, Multifector 213252-23-4, Superfect
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT 264232-01-1 264252-63-3 264252-64-4 264252-65-5 264252-66-6 264252-67-7 264252-68-8 264252-69-9 264252-70-2 264252-72-4 264252-73-5 264252-74-6 264252-75-7 264252-76-8 264252-77-9 264252-78-0 264252-79-1 264252-80-4 264252-81-5 264252-82-6 264252-83-7 264252-84-8 264252-85-9 264252-86-0 264252-87-1

264261-81-6 264261-82-7 264261-83-8 264261-84-9 264261-85-0
264261-86-1 264261-87-2 264261-88-3 264261-90-7 264261-91-8
264261-92-9 264261-93-0 264261-94-1 264261-95-2 264261-96-3
264261-98-5 264261-99-6 264262-00-2 264262-02-4 264262-10-4
264262-18-2 264262-24-0 264262-30-8 264262-33-1 264262-37-5
264264-41-7 264264-66-6 264264-80-4 264264-91-7 264265-38-5
264266-32-2 264266-43-5 264266-59-3 264266-67-3 264271-84-3
264271-85-4 264271-86-5 264271-87-6 264272-18-6 264272-20-0
RL: PRP (Properties)
(unclaimed **protein** sequence; peptide-enhanced cationic lipid transfections)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:84648 CAPLUS
DOCUMENT NUMBER: 132:141941
TITLE: **Conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders
INVENTOR(S): Mcdonald, John R.; Coggins, Philip J.
PATENT ASSIGNEE(S): Osprey Pharmaceuticals Limited, Can.
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004926	A2	20000203	WO 1999-CA659	19990721
WO 2000004926	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335105	AA	20000203	CA 1999-2335105	19990721
AU 9948918	A1	20000214	AU 1999-48918	19990721
EP 1098664	A2	20010516	EP 1999-932572	19990721
EP 1098664	B1	20030806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002521019	T2	20020716	JP 2000-560919	19990721
AT 246517	E	20030815	AT 1999-932572	19990721
EP 1346731	A1	20030924	EP 2003-76150	19990721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2002168370	A1	20021114	US 2001-792793	20010222
HK 1037133	A1	20031107	HK 2001-107546	20011030
US 2003215421	A1	20031120	US 2003-375209	20030224

PRIORITY APPLN. INFO.:

US 1998-120523	A2	19980722
US 1998-155186P	P	19980722
EP 1999-932572	A3	19990721
WO 1999-CA659	W	19990721

US 1999-360242 A3 19990722
US 1999-453851 A3 19991202
US 2001-792793 A1 20010222

AB **Conjugates** containing as a ligand a chemokine receptor-targeting agent, such as chemokines, and a targeted agent, such as a toxin are provided. These **conjugates** are used to treat inflammatory responses associated with activation, proliferation and migration of immune effector cells, including leukocyte cell types, neutrophils, macrophages, and eosinophils. The **conjugates** provided herein are used to lessen or inhibit these processes to prevent or at least lessen the resulting secondary effects. In particular, the **conjugates** are used to target toxins to receptors on secondary tissue damage-promoting cells. The ligand moiety can be selected to deliver the cell toxin to such secondary tissue damage-promoting cells as mononuclear phagocytes, leukocytes, natural killer cells, dendritic cells, and T and B lymphocytes, thereby suppressing the proliferation, migration, or physiol. activity of such cells. Among preferred **conjugates** are fusion proteins having a chemokine, or a biol. active fragment thereof, as the ligand moiety **linked** to a cell toxin via a peptide **linker** of from 2 to about 60 amino acid residues.

IC ICM A61K047-48

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 15

ST antiinflammatory drug targeting fusion **protein** chemokine toxin sequence

IT AIDS (disease)
AIDS (disease)
(AIDS dementia complex; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Mental disorder
Mental disorder
(AIDS dementia; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(CTAP III, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Intestine, disease
(Crohn's; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ENA-78, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GCP-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GRO-α, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GRO-β, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GRP-γ, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(IP-10, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Kidney, disease
(IgA nephropathy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(LAPF-4, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lipoprotein receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(LDL; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(MIP-3, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(Mig (monokine induced by interferon-γ), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(NAP-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(PBP, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), bryodins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), dianthin 30, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), dianthin 32, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), lychnin, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RIP (ribosome-inactivating **protein**), mapalmin, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Barley
Corn
Flax
(RIP of; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Arthritis
(Reiter's syndrome; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SDF-1α (stromal-derived factor-1α), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SDF-1β (stromal-derived factor-1β), **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SDF-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(Shiga; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(adenocarcinoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Brain, disease
(adrenoleukodystrophy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Respiratory distress syndrome
(adult; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Spinal column
(ankylosing spondylitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Nutrients
(anti-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antiarteriosclerotics

(antiatherosclerotics; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Aspergillus
(aspergillosis from; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Astrocyte
Astrocyte
(astrocytoma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(astrocytoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lung, disease
(bronchopulmonary dysplasia; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Nervous system
(central, inflammation; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Nervous system
(central, injury; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Fusion **proteins** (chimeric **proteins**)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chemokine receptor-binding; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(chemokine receptor-binding; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Leukocyte
(chemokine receptors of; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Meningitis
(chorio-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Eye, disease
(choroiditis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Fatigue, biological
(chronic fatigue syndrome; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Intestine, disease
(colitis, chronic; **conjugates** and fusion **proteins**

for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Alzheimer's disease
Anti-inflammatory agents
Antiarthritics
Antiparkinsonian agents
Antirheumatic agents
Antitumor agents
Atherosclerosis
B cell (lymphocyte)
Basophil
Behcet's syndrome
Bronchodilators
Cell migration
Cell proliferation
Coupling agents
Dendritic cell
Down's syndrome
Drug targeting
Encephalitis
Encephalomyelitis
Eosinophil
Genetic vectors
Granuloma
Heart, disease
Hodgkin's disease
Immunosuppressants
Inflammation
Molecular cloning
Multiple sclerosis
Neutrophil
Osteoarthritis
Parkinson's disease
Plasmid vectors
Pneumonia
Protein sequences
Sarcoidosis
T cell (lymphocyte)
Venoms
cDNA library
cDNA sequences
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Fusion **proteins** (chimeric **proteins**)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Abrins
Ricins
Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and

disorders)
IT Nucleic acids
RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Interleukin 3
Macrophage inflammatory **protein** 2
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT G **protein**-coupled receptors
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Primers (nucleic acid)
RL: PRP (Properties)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Trichosanthin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Eotaxin
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Interleukin 1
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Interleukin 12
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Interleukin 13
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**

for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Interleukin 2
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Interleukin 4
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Interleukin 5
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Interleukin 6
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Interleukin 8
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Macrophage inflammatory **protein** 1α
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Macrophage inflammatory **protein** 1β
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Monocyte chemoattractant **protein**-1
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins**
for treating secondary tissue damage and other inflammatory conditions and disorders)

IT RANTES (chemokine)
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP

(Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Neoplasm
(cytokine-regulated; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Nervous system
(degeneration; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Eye, disease
(diabetic retinopathy, proliferative; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(diphtheria; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lung, disease
Pneumonia
(eosinophilic; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Pseudomonas
(exotoxin; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(exotoxins, of Pseudomonas; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lung, disease
(fibrosis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fusion **proteins**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fusion-**protein** ligands for; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Neuroglia
Neuroglia

(glioblastoma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(glioblastoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Neuroglia
Neuroglia
(glioma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(glioma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Kidney, disease
(glomerulonephritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Eye, disease
Joint, anatomical
Lung, disease
(inflammation; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Intestine, disease
(inflammatory; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lung, neoplasm
Lung, neoplasm
(inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(injections, i.m.; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(injections, i.p.; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(injections, i.v.; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(injections, intraarticular; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(injections, intracisternal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(injections, intradermal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems

(injections, intraventricular; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Spinal cord
(injury; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(intratracheal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Rheumatoid arthritis
(juvenile; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(leukemia; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Brain, disease
(leuko-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Peptides, properties
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(**linkers**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Drug delivery systems
(local; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
Antitumor agents
(lung; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Kidney, disease
(lupus nephritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(lymphoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(macrophage inflammatory **protein**, γ, **conjugates** ; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(mammary gland; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(melanoma; **conjugates** and fusion **proteins** for

treating secondary tissue damage and other inflammatory conditions and disorders)

IT Meninges
(meningioma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Neuroglia
(microglia, microglioma inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(momordins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antibodies
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(monoclonal; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein** 3, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein** 4, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein** 5, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant **protein**-2, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Phagocyte
(mononuclear; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Antitumor agents
(myeloma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Lymphocyte
(natural killer cell; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Mammary gland
Mammary gland
Prostate gland
Prostate gland
(neoplasm, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Kidney, disease
(nephritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Neuroglia
Neuroglia
(oligodendroglioma, inhibitors; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Antitumor agents
(oligodendroglioma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Drug delivery systems
(ophthalmic; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Nose
(polyposis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Antitumor agents
(prostate gland; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Arthritis
(psoriatic arthritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Arthritis
(reactive; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Eye, disease
(retinitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Nose
(rhinitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(saporins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Antitumor agents

(sarcoma; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Eye, disease
(scleritis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Respiratory tract
(sinusitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Venoms
(snake; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Spinal column
(spondyloarthropathy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Brain, disease
(spongiform encephalopathy; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Brain, disease
(stroke; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Drug delivery systems
(targeted; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Thyroid gland, disease
(thyroiditis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Drug delivery systems
(topical; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Bacteria (Eubacteria)
Insect (Insecta)
Plant (Embryophyta)
Spider
(toxins of; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Intestine, disease
(ulcerative colitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Biological transport
(uptake; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Eye, disease
(uveitis; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)
IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α-momorcharins, **conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Macroglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α2-; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(β-momorcharins; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 51-17-2, Benzimidazole 84-65-1, Anthraquinone 120500-15-4, Leinamycin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**DNA**-cleaving; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 256633-15-5P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 50-07-7, Mitomycin c 51-21-8, 5-Fluorouracil 55-86-7, Nitrogen mustard 59-05-2, Methotrexate 148-82-3, Melphalan 11000-04-7D, Colicin, **conjugates** 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 65988-88-7, Modeccin 75037-46-6D, Gelonin, **conjugates** 91933-11-8, Volkensin 95787-44-3D, Dodecandrin, **conjugates** 160674-53-3D, Luffin a, **conjugates** 160674-54-4D, Luffin b, **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 9003-98-9, Dnase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 81627-83-0, Mcsf 83869-56-1, Gmcsf 143011-72-7, Gcsf
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions

and disorders)

IT 69-78-3 15791-08-9 68181-17-9 72252-96-1 88442-68-6, S-(2-Pyridylthio)-L-cysteine **106145-13-5** 115616-51-8 150244-18-1 158913-22-5 160854-54-6 199804-25-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(cross-**linker**; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 256633-14-4P
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(**nucleotide** sequence; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 203780-20-5 225895-00-1 256633-43-9, 7: PN: WO0004926 SEQID: 40 unclaimed **DNA** 256633-44-0, 8: PN: WO0004926 SEQID: 41 unclaimed **DNA** 256633-45-1, 9: PN: WO0004926 SEQID: 42 unclaimed **DNA** 256633-46-2 256633-47-3 256633-48-4 256633-49-5 256633-50-8 256633-51-9 256633-52-0 256633-53-1 256633-54-2 256633-55-3 256633-56-4 256633-57-5 256633-58-6 256633-59-7 256633-60-0 256633-61-1 256633-62-2 256633-63-3 256633-64-4 256633-65-5 256633-66-6 256633-67-7 256633-68-8 256633-69-9
RL: PRP (Properties)
(unclaimed **nucleotide** sequence; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 2543-43-3 99283-10-0, Colony-stimulating factor 2 (human clone pHG25 **protein** moiety reduced) 102619-52-3, Lymphokine MIP 1α (human clone pLD78 macrophage inflammatory reduced) 104950-39-2, Interleukin 4 (human clone 46 **protein** moiety reduced) 111906-18-4, Interleukin 3 (human clone D11 **protein** moiety reduced) 112002-52-5, Toxin (Shigella dysenteriae A-subunit reduced) 112487-62-4, Interleukin 8 (human clone 3-10C reduced) 112871-94-0, Toxin SLT-II (bacteriophage 933W A-subunit precursor reduced) 117216-60-1, **Protein** (human T-lymphocyte gene RANTES reduced) 118899-93-7, Melanoma growth stimulatory activity (human clone pMGSA5-2/3 isoform α reduced) 121853-02-9, Lymphokine MIP 1β (human clone pAT744 macrophage inflammatory reduced) 124147-31-5, Lymphokine MCP 1 (human **protein** moiety reduced) 124760-57-2, **Protein** MAP (Mirabilis jalapa clone pMH2 reduced) 128794-97-8, Trichosanthin (Trichosanthes kirilowii strain Maximowicz) 130838-28-7 131199-57-0, Lymphokine MIP 2β (human clone hMIP-2-4a macrophage inflammatory reduced) 131199-58-1, Lymphokine MIP 2α (human clone hMIP-2-5a macrophage inflammatory reduced) 141961-54-8, **Protein** (human sialoglycoprotein LRP-associated) 143973-96-0, Cytokine (human clone NC28 **protein** moiety reduced) 150243-58-6 150243-59-7 153177-60-7 188204-50-4, 24-270-Bryodin 1 (Bryodin dioica) 189582-41-0 189704-25-4, Eotaxin (human clone pVL141) 194675-15-5, Dendrokine (human clone SHO46) 197665-51-3 256633-70-2 256633-71-3 256633-72-4 256633-73-5 256649-82-8 256649-85-1
RL: PRP (Properties)
(unclaimed **protein** sequence; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

IT 256504-33-3 256504-34-4 256504-35-5 256504-36-6 256504-37-7
RL: PRP (Properties)
(unclaimed sequence; **conjugates** and fusion **proteins** for treating secondary tissue damage and other inflammatory conditions and disorders)

L31 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:521100 CAPLUS
DOCUMENT NUMBER: 131:308434
TITLE: A Multistep Chemical Modification Procedure To Create **DNA** Arrays on Gold Surfaces for the Study of **Protein-DNA** Interactions with Surface Plasmon Resonance Imaging
AUTHOR(S): Brockman, Jennifer M.; Frutos, Anthony G.; Corn, Robert M.
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, WI, 53706-1396, USA
SOURCE: Journal of the American Chemical Society (1999), 121(35), 8044-8051
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A multistep surface modification procedure for the creation of DNA arrays on chemical modified gold surfaces that can be used in surface plasmon resonance (SPR) imaging studies of protein-DNA interactions is demonstrated. The multistep procedure is required to create an array of spots that are surrounded first by a hydrophobic background which allows for the pinning of aqueous DNA solns. onto individual array elements and then to replace that hydrophobic background with one that resists the nonspecific adsorption of proteins during in situ SPR imaging measurements. An **amine**-terminated alkanethiol monolayer is employed as the base layer, and Fmoc and PEG **modifiers** are used to create the sequentially hydrophobic and protein adsorption-resistant surfaces, resp. Specifically, the chemical **modification** steps are the following: (1) the adsorption and self-assembly of an 11-mercaptoundecylamine (MUAM) monolayer on an evaporated gold thin film, (2) the reaction of the MUAM monolayer with an Fmoc protecting group to create a hydrophobic surface, (3) the photopatterned removal of the alkanethiol followed by (4) the readsorption of MUAM to create an array of MUAM squares (750+750 μm) surrounded by a hydrophobic MUAM-Fmoc background that can pin drops of aqueous solution, (5) the attachment of **oligonucleotide** sequences onto the MUAM squares by the reaction of the **amine**-terminated surface with the heterobifunctional cross linker SSMCC followed by a coupling reaction to a small volume (0.1 μL) of thiol-**modified DNA**, and (6) the removal of the Fmoc protecting group followed by (7) a pegylation reaction of the MUAM with PEG-NHS to create a protein adsorption-resistant background. A combination of polarization-modulation FTIR spectroscopy, contact angle, and scanning angle SPR measurements is used to characterize the surface modification procedure. An SPR imaging measurement of the adsorption of single-stranded DNA binding protein (SSB) onto an oligonucleotide array created by this procedure is used to demonstrate the utility of these surfaces.

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 6.
ST **DNA** array chip **protein** recognition surface plasmon resonance imaging
IT Analytical apparatus
(**DNA** arrays on gold surface, supported by silanized microscope slide covers; multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)
IT **Proteins**, specific or class

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(SSB (single-stranded **DNA**-binding); multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT Imaging
Molecular recognition
Self-assembled monolayers
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT **Proteins**, general, analysis
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT **DNA**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT **Oligonucleotides**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT Adsorption
(**protein**; multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT Surface plasmon
(resonance; multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT 247247-38-7 247247-40-1
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT 7440-57-5, Gold, uses
RL: DEV (Device component use); USES (Uses)
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

IT 82911-69-1 **103708-09-4**, **Sulfo-SMCC**
130727-41-2 155638-19-0
RL: DEV (Device component use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(multistep chemical modification procedure to create **DNA** arrays on gold surfaces for study of **protein-DNA** interactions with surface plasmon resonance imaging)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:719089 CAPLUS
DOCUMENT NUMBER: 129:341449
TITLE: Active microtubule-based separations by kinesins

INVENTOR(S): Stewart, Russell J.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 24 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5830659	A	19981103	US 1996-713815	19960913

PRIORITY APPLN. INFO.: US 1996-713815 19960913

AB A method and system for separating a selected mol. from a heterogeneous mixture of mols. in aqueous solution are described. The method comprises (a) providing a separation device comprising a loading reservoir and a receiving reservoir coupled by a channel bearing immobilized microtubules aligned parallel to the longitudinal axis of the channel; (b) placing an aqueous solution containing the heterogeneous mixture of mols. in the loading reservoir; (c) adding a motor-ligand composition and ATP to the aqueous solution, wherein the motor-ligand composition comprises a motor protein for attaching to microtubules and moving therealong in the presence of ATP and the ligand is capable of binding the selected mol., such that the ligand binds the selected mol. to form a complex and the complex moves along the immobilized microtubules to the receiving reservoir; and (d) removing the selected mol. from the receiving chamber. Thus, a separation device was prepared by photolithog. etching of a glass substrate. The channel separating the loading and receiving chambers was derivatized with trimethoxysilylpropyldiethylenetriamine. A fraction of the surface amino groups were then reacted with **sulfosuccinimidyl** -(4-azidosalicylamido)-hexanoate. Microtubules were aligned in the channel by flow alignment. Microtubules electrostatically bound to the channel surface were crosslinked to the surface by UV irradiation Then a solution containing ATP and phage λ and plasmid pBR322 was placed in the reservoir. A kinesin-cos site-binding oligonucleotide conjugate was then added to the reservoir. There was separation of λ DNA from pBR322 DNA because active transport of λ DNA to the receiving reservoir is more rapid than diffusion of the pBR322 DNA.

IC ICM C12Q001-68
ICS C12Q001-34; G01N033-566; C12M001-40
NCL 435006000
CC 9-9 (Biochemical Methods)
IT **Oligonucleotides**
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates** with motor **proteins**; active microtubule-based sepns. by kinesins)
IT 215378-84-0D, **conjugates** with **oligonucleotides** and fusion **proteins** with streptavidin 215378-85-1D, **conjugates** with **oligonucleotides** and fusion **proteins** with streptavidin
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(**amino** acid sequence; active microtubule-based sepns. by kinesins)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:621324 CAPLUS
DOCUMENT NUMBER: 129:240848
TITLE: Increasing the efficiency of uptake of transforming **DNA** complexes with polycations using peptides
INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Ciccarone, Valentina C.; Evans, Krista L.; Schifferli, Kevin P.; Gebeyehu, Guililat
PATENT ASSIGNEE(S): Life Technologies, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840502	A1	19980917	WO 1998-US5232	19980316
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6051429	A	20000418	US 1997-818200	19970314
AU 9865622	A1	19980929	AU 1998-65622	19980316
EP 1007699	A1	20000614	EP 1998-911737	19980316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517939	T2	20011009	JP 1998-539899	19980316

PRIORITY APPLN. INFO.:
US 1997-818200 A 19970314
US 1995-477354 B2 19950607
US 1996-658130 A2 19960604
WO 1998-US5232 W 19980316

AB A method of increasing the efficiency of transformation of eukaryotic cells using complexes of nucleic acids with polycations is decribed. The method uses peptide **conjugates** with nucleic acid-binding moieties, cationic lipids and dendrimers to complex the DNA. The peptides may be synthetic or derived from a cellular protein and may be further derivatized, e.g. by selective deprotection. The peptide may also be covalently **linked** to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection compns. or covalent attachment of peptides to transfection agents increases the efficiency of transfection. Methods for the preparation of transfection compns. and methods of using these transfection compns. as intracellular delivery agents and extracellular targeting agents are also disclosed.

IC ICM C12N015-64
ICS C12N015-63; C07K014-00; G01N033-92

CC 3-1 (Biochemical Genetics)

ST peptide polycation **DNA** complex transformation efficiency; polyamine peptide **DNA** complex transformation efficiency; spermine peptide **DNA** complex transformation efficiency

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(BPI (bactericidal/permeability-increasing), increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Glycoproteins, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Semliki forest virus, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Toxins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Shiga, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(VP22, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Lipids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cationic, in transformation; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **DNA**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(complexes, **conjugates**; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Toxins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(diphtheria, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Toxins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(endotoxins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusogenic, increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hepatitis B core, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hexon, increasing efficiency of transformation with peptides of;

increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Cell adhesion molecules
Fibronectins
High-mobility group **proteins**
Histones
Lactoferrins
Transferrins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Transformation, genetic
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Hemagglutinins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(influenza virus, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(internalins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(invasins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(knob, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nucleic acid-binding, peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **Proteins**, specific or class
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(penton base, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptides and ligands of, increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Adenoviridae
Alphavirus
Hepatitis virus
Herpesviridae
Human immunodeficiency virus
Influenza virus
Semliki Forest virus
Vesicular stomatitis virus
(peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Polyamines
Polyamines
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamide-, transformation using, increasing efficiency of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Polyamides, biological studies
Polyamides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamine-, transformation using, increasing efficiency of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Amines, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamines, nonpolymeric, complexes with **DNA**; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Transcription factors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tat, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Protamines
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(thionins, increasing efficiency of transformation with peptides of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Animal cell
Fibroblast
(transformation of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT Dendritic polymers
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT **92921-26-1**, **Sulfo-SMPB**
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation spermine-containing peptides; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)

IT 213131-54-5P 213131-55-6P 213131-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in preparation spermine-containing peptides; increasing efficiency of uptake of
transforming **DNA** complexes with polycations using peptides)
IT 9004-10-8D, Insulin, peptides, biological studies 62031-54-3D, Fibroblast growth factor, peptides 62229-50-9D, Epidermal growth factor, peptides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
IT 1405-97-6D, Gramicidin, peptides 1414-45-5D, Nisin, derivs., peptides 37231-28-0D, Melittin, derivs., peptides 80802-79-5D, Cecropin, peptides 103220-14-0D, Defensin, peptides 113041-69-3D, Magainin, derivs., peptides 116229-36-8D, Bactenecin, derivs., peptides 123997-21-7D, Apidaecin, derivs., peptides 140896-21-5D, Indolicidin, derivs., peptides 148045-87-8D, Tachyplesin, peptides 163663-18-1D, Protegrin, peptides 170006-50-5D, Cathelicidin, derivs., peptides 173010-28-1D, Buforin I, derivs., peptides 182970-24-7D, Drosomycin, derivs., peptides 213131-57-8 213131-71-6 213131-72-7 213131-74-9 213131-76-1 213131-78-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of transformation with; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
IT 71-44-3D, Spermine, peptide **conjugates**, complexes with nucleic acids
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
IT 2462-63-7, Lipofectace 124050-77-7, DOGS 158571-62-1, Lipofectamine 163442-69-1D, Starburst 6th generation, **conjugates** with lysine or arginine 163442-70-4D, Starburst 7th generation, **conjugates** with lysine or arginine 163442-72-6D, Starburst 9th generation, **conjugates** with lysine or arginine 168479-03-6, DOSPA 178532-92-8, DOSPER 189203-04-1, Cellfectin 189203-05-2, DMRIE-C 213131-59-0 213131-62-5 213131-65-8 213131-68-1 213131-69-2 213186-72-2, DMRIE-DOPE mixture 213252-20-1, Multifector 213252-23-4, Superfect
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation using, increasing efficiency of; increasing efficiency of uptake of transforming **DNA** complexes with polycations using peptides)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:572338 CAPLUS
DOCUMENT NUMBER: 129:186415
TITLE: Detection of targets with green fluorescent **protein** and fluorescent variants thereof
INVENTOR(S): Plaia, Todd W.
PATENT ASSIGNEE(S): Oncor, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836099	A1	19980820	WO 1998-US3147	19980218
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9866588	A1	19980908	AU 1998-66588	19980218
EP 1000172	A1	20000517	EP 1998-908588	19980218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001514741	T2	20010911	JP 1998-536010	19980218
PRIORITY APPLN. INFO.:			US 1997-38623P P	19970218
			WO 1998-US3147 W	19980218

AB A labeled marker for detection of a target is described which includes a label selected from the group consisting of green fluorescent protein and a fluorescent variant thereof, and a ligand configured to bind to the target. The ligand includes any mol. or combination of mols. which have an affinity for another substance. For example, the ligand can be selected from the group consisting of nucleic acid probe, antibody, hapten **conjugate**, biotin, avidin and streptavidin. A method for detecting a target is also described which includes providing a primary ligand configured to bind to the target and providing a secondary ligand configured to bind to the primary ligand. Techniques such as fluorescent microscopy are used to visualize the labeled marker.

IC ICM C12Q001-68
ICS G01N033-53; C12P021-04; C12N009-02; C07K001-00; C07H019-04; C07H021-04

CC 9-5 (Biochemical Methods)
Section cross-reference(s): 3, 6

ST green fluorescent **protein** ligand marker binding; fluorescence
green fluorescent **protein** ligand marker

IT Azides
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(aryl; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Gene, animal
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(c-erbB2; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Ligands
RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(**conjugated**, with green fluorescent **protein** variants; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Avidins
Haptens
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL

(Biological study); PROC (Process)
(**conjugates**, with green fluorescent **protein**; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Staining, biological
(counterstain; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT **Crosslinking**
Crosslinking agents
Fluorescent probes
Fluorescent substances
Fluorometry
Genetic mapping
Immunoassay
Molecular association
Nucleic acid hybridization
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Carbohydrates, analysis
DNA
Proteins, general, analysis
RNA
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Alkyl halides
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Aryl halides
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(green fluorescent; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Acetals
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(halo-; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Chromosome
(human 17; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Chromosome
(human Y; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Esters, analysis
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological

study); RACT (Reactant or reagent); USES (Uses)
(imides; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Nucleic acid hybridization
(in situ, fluorescence; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Nucleic acid hybridization
(in situ; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Antibodies
Probes (nucleic acid)
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(labeled with green fluorescent **protein**; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT Fluorescent indicators
(marker; detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT 25535-16-4, Propidium iodide 47165-04-8, DAPI
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT 58-85-5D, Biotin, labeled with green fluorescent **protein**
1672-46-4, Digoxigenin 9013-20-1D, Streptavidin, labeled with green fluorescent **protein**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

IT 107-22-2, Glyoxal 151-51-9, Carbodiimide 541-59-3, Maleimide 6066-82-6D, N-Hydroxysuccinimide, esters 35013-72-0, Biotin N-hydroxysuccinimide ester 73370-52-2, Pyridine, dithiobis 76931-93-6, N-Succinimidyl S-acetylthioacetate **103708-09-4**, **Sulfo-SMCC**
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(detection of targets with green fluorescent **protein** and fluorescent variants thereof)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:475105 CAPLUS
DOCUMENT NUMBER: 127:106361
TITLE: Preparation of photoprotein **conjugates** and methods of use thereof
INVENTOR(S): Stults, Nancy L.
PATENT ASSIGNEE(S): Sealite Sciences, Inc., USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 5,486,455.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5648218	A	19970715	US 1995-465791	19950606
US 5486455	A	19960123	US 1994-293648	19940822
PRIORITY APPLN. INFO.:			US 1993-117116 B1	19930813
			US 1994-293648 A2	19940822
			US 1993-17116 B1	19930212

AB The present invention encompasses a method of synthesis of **conjugates** of photoproteins that retain all or a substantial portion of the luminescent activity of underivatized photoprotein. According to the present invention photoproteins may be **conjugated** with a variety of binding reagents including streptavidin/avidin, glycoproteins, lectins, hormones, antigens, drugs, antibodies and antigen-binding fragments thereof, or any other selectively bindable reagent by chemical **crosslinking** means. The present invention also encompasses **conjugates** produced by this method and methods of use of such **conjugates.**

IC ICM C12Q001-68
ICS C12Q001-70; G01N033-53; C07H021-04

NCL 435006000

CC 9-15 (Biochemical Methods)

ST aequorin **conjugate**; avidin photoprotein **conjugate**; glycoprotein photoprotein **conjugate**; lectin photoprotein **conjugate**; hormone photoprotein **conjugate**; antigen photoprotein **conjugate**; antibody photoprotein **conjugate** ; drug photoprotein **conjugate**

IT Aequorins
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(apoaequorins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(apoberovins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(apomnemiopsins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(apoobelins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(clytins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(halistovein thalassiciolins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(mnemiopsins; preparation of photoprotein **conjugates** and methods of use thereof)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(obelins; preparation of photoprotein **conjugates** and methods of use thereof)
IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(photoproteins; preparation of photoprotein **conjugates** and methods of use thereof)
IT Aequorins
Agglutinins and Lectins
Antibodies
Antigens
Avidins
Drugs
Enzymes, reactions
Glycoproteins, specific or class
Hormones, animal, reactions
Oligonucleotides
Peptides, reactions
Receptors
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(preparation of photoprotein **conjugates** and methods of use thereof)
IT 9013-20-1, Streptavidin 96827-88-2, Pholasin
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(preparation of photoprotein **conjugates** and methods of use thereof)
IT 4856-87-5, Bis(maleimido)hexane 6539-14-6, 2-Iminothiolane 6953-60-2, S-Acetylmercaptosuccinic anhydride 15209-14-0, Bis(maleimido) methyl ether 58626-38-3 64987-85-5, SMCC 79886-55-8 80307-12-6, GMBS 83306-17-6, N-Succinimidyl-3-(2-pyridylthio)propionate **92921-26-1**, **Sulfo-SMPB 103708-09-4**, **Sulfo-SMCC 185332-92-7**, **Sulfo-GMBS**
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of photoprotein **conjugates** and methods of use thereof)

L31 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:130043 CAPLUS
DOCUMENT NUMBER: 126:127859
TITLE: Use of biologically active peptides to increase the efficiency of transformation with **DNA**:cationic lipid complexes
INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.
PATENT ASSIGNEE(S): Life Technologies, Inc., USA; Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9640961	A1	19961219	WO 1996-US8723	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9659792	A1	19961230	AU 1996-59792	19960604
EP 874910	A1	19981104	EP 1996-917118	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 11506935	T2	19990622	JP 1996-501227	19960604
PRIORITY APPLN. INFO.:			US 1995-477354 A	19950607
			WO 1996-US8723 W	19960604

AB Biol. active peptides, such as receptor ligands, fusogenic peptides, or nuclear localization signals are incorporated into complexes of DNA and cationic lipids to increase the effectiveness of transformation of eukaryotic cells. These peptides may also be **conjugated** with a DNA-binding peptide or group such as spermine. Methods for the preparation of transfecting compns. and use as intracellular delivery agents and extracellular targeting agents are also disclosed. Transformation efficiencies of animal cell lines with LipofectAMINE® liposomes were increased by up to .apprx.50-fold when **conjugates** of viral RGD peptides and spermine were added to the complex.

IC ICM C12N015-88
ICS C12N007-04; C07H021-00

CC 3-1 (Biochemical Genetics)

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HN (hemagglutinin-neuraminidase), fusogenic peptides of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT **Proteins**, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(NLS (nuclear location signal sequence)-containing, peptides of, in liposome transformations; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Lipids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cationic and neutral, transformation with liposomes containing; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Alphavirus
Influenza virus
Vesicular stomatitis virus
(fusogenic peptides of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fusogenic, in liposome transformations; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(large T, nuclear localization peptides of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Simian virus 40
(nuclear localization peptides of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Transformation, genetic
(of eukaryotic cells; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide ligands for, in liposome transformations; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT **Amines**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyamines, nonpolymeric, effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT Fibroblast
(transformation of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 71-44-3D, Spermine, peptide **conjugates**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**DNA** binding by; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 95214-35-0 117138-20-2 127258-60-0 127258-63-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(**amino** acid sequence, effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 186451-48-9P 186451-51-4P 186451-54-7P 186451-56-9P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**amino** acid sequence, effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT **92921-26-1**, **Sulfo-SMPB**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** of peptides and spermine using; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 25104-18-1, Polylysine 38000-06-5, Polylysine
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effects on LipofectAMINE-mediated transformation efficiency of; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 186451-46-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and reactions of, in **conjugation** of **proteins** with spermine; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 2462-63-7, Dioleoylphosphatidylethanolamine 185097-43-2
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation with liposomes containing; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

IT 158571-62-1, Lipofectamine
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(transformation with; use of biol. active peptides to increase efficiency of transformation with **DNA**:cationic lipid complexes)

L31 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:610222 CAPLUS
DOCUMENT NUMBER: 125:269866
TITLE: CAP-phenanthroline conjugate for DNA cleavage
INVENTOR(S): Ebright, Richard H.; Ebright, Y. W.; Pendergrast, P. Shannon
PATENT ASSIGNEE(S): Rutgers University, USA
SOURCE: U.S., 12 pp., Cont. of U.S. Ser. No. 124,362,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5556949	A	19960917	US 1994-320568	19941011

PRIORITY APPLN. INFO.: US 1991-747731 19910820
US 1993-124362 19930920
OTHER SOURCE(S): MARPAT 125:269866

AB A class of site-specific **DNA** cleavage agents is disclosed comprising a sequence-specific **DNA**-binding protein (i.e., catabolite gene-activator protein, CAP) and a nucleolytic moiety (i.e., 1,10-phenanthroline derivative) attached thereto at an **amino** acid that is close to **DNA** in the specific protein-**DNA** complex but that is not close to **DNA** in the nonspecific protein-**DNA** complex. These site-specific DNA cleavage agents cleave DNA at specific DNA recognition sites and have little or no nonspecific DNA cleavage activity.

IC ICM C07K001-107
ICS C07D471-02; C12Q001-68
NCL 530402000
CC 9-15 (Biochemical Methods)
Section cross-reference(s): 3, 6, 67
ST **DNA** cleavage agent CAP phenanthroline **conjugate**; catabolite gene activator **protein DNA** cleavage
IT Ribonucleic acid formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); CAT (Catalyst use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(CAP (catabolite gene activator **protein**), **conjugates** with phenanthroline derivs.; CAP-phenanthroline **conjugate** for

DNA cleavage)
IT 182685-69-4DP, CAP **protein conjugates** 182685-70-7DP, CAP **protein conjugates** 182685-71-8DP, CAP **protein conjugates**
RL: BPR (Biological process); BSU (Biological study, unclassified); CAT (Catalyst use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(CAP-phenanthroline **conjugate** for **DNA** cleavage)
IT 598-21-0, Bromoacetyl bromide 4199-88-6, 5-Nitro-1,10-phenanthroline 12135-76-1, Ammonium **sulfide** 54907-61-8, Iodoacetic anhydride 182087-16-7, GenBank I26206
RL: RCT (Reactant); RACT (Reactant or reagent)
(CAP-phenanthroline conjugate for DNA cleavage)
IT 54258-41-2P, 5-**Amino**-1,10-phenanthroline 111047-29-1P 152572-68-4P 154030-81-6P 182685-66-1P 182685-67-2P 182685-68-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(CAP-phenanthroline conjugate for **DNA** cleavage)

L31 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:328936 CAPLUS
DOCUMENT NUMBER: 122:306484
TITLE: Properties of exonuclease-resistant, psoralen-conjugated oligodeoxyribonucleotides in vitro and in cell culture
AUTHOR(S): Levis, Joel T.; Miller, Paul S.
CORPORATE SOURCE: School Hygiene Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA
SOURCE: Antisense Research and Development (1994), 4(4), 231-41
CODEN: AREDEI; ISSN: 1050-5261
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have prepared **oligodeoxyribonucleotides** that are **modified** at the 3'-terminal with N4-(4-aminobutyl)deoxycytidine and derivatized at the 5'-end with a 4'-([N-(aminoethyl)**amino**]methyl)-4,5',8-trimethylpsoralen [(ae)AMT] and whose sequences are complementary to vesicular stomatitis virus (VSV), N-protein mRNA [(ae)AMT-II] or VSV M-protein mRNA [(ae)AMT-III]. (Ae)AMT-II cross-links exclusively to VSV N-mRNA when a mixture of the oligomer and poly(A+) RNA from VSV-infected cells is irradiated in vitro with long wavelength UV light at either 20° or 37°. N4-(4-Aminobutyl)deoxycytidine at the 3'-end of (ae)AMT-II does not appear to affect the binding or crosslinking of the oligomer to its target RNA. Oligomer (ae)AMT-II is completely resistant to hydrolysis by the 3'-5'-exonuclease activity found in fetal calf serum whereas a similar oligomer [(ae)AMT-I] which contains a 3'-terminal deoxycytidine, is hydrolyzed within 30 min when incubated at 37°. Intact (ae)AMT-II was found in both the cell lysate and cell culture medium after 12 h of incubation with mouse L-cells along with d-(ae)AMTpT, which appears to result from endonuclease degradation of the oligomer. In contrast, no intact (ae)AMT-I was found in either the cell lysate or the culture medium after 1 h incubation. Although 10 μM (ae)AMT-II had no effect on VSV-protein synthesis in either unirradiated or UV-irradiated VSV-infected mouse L-cells, 10 μM (ae) AMT-III inhibited VSV protein synthesis 30% in irradiated cells. These results show that introduction of a N4-(4-aminobutyl)deoxycytidine at the 3'-end of an oligodeoxyribonucleotide significantly increases the resistance of the oligomer to degradation by 3',5'-exonucleases but does not interfere with its ability to bind selectively to complementary RNA. Further

derivatization with psoralen creates an oligomer that can be triggered to cross-link with RNA in a sequence-specific manner, is taken up intact by mammalian cells in culture, and exhibits biol. activity. In combination, these two modifications endow the oligodeoxyribonucleotide with novel properties that could be exploited in the design of antisense or antigene reagents for use in controlling gene expression in mammalian cells.

CC 1-12 (Pharmacology)
Section cross-reference(s): 8, 33

IT **Nucleotides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oligo-, deoxyribo-, antisense; properties of exonuclease-resistant and psoralen-**conjugated** antisense oligodeoxyribonucleotides in vitro and in cell culture in relation to vesicular stomatitis virus **protein** synthesis inhibition)

L31 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:625876 CAPLUS
DOCUMENT NUMBER: 121:225876
TITLE: Preparation of photoprotein **conjugates** and methods of use thereof
INVENTOR(S): Stults, Nancy L.
PATENT ASSIGNEE(S): Sealite Sciences, Inc., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9418342	A1	19940818	WO 1994-US1387	19940204
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9461718	A1	19940829	AU 1994-61718	19940204
EP 683822	A1	19951129	EP 1994-908734	19940204
EP 683822	B1	20020502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08506897	T2	19960723	JP 1994-518303	19940204
AT 217086	E	20020515	AT 1994-908734	19940204
IL 108607	A1	19981206	IL 1994-108607	19940209

PRIORITY APPLN. INFO.: US 1993-17116 A 19930212
WO 1994-US1387 W 19940204

AB The present invention encompasses a method of synthesis of **conjugates** of photoproteins that retain all or a substantial portion of the luminescent activity of underivatized photoprotein. According to the present invention photoproteins may be **conjugated** with a variety of binding reagents including streptavidin/avidin, glycoproteins, lectins, hormones, antigens, drugs, antibodies and antigen binding fragments thereof, or any other selectively bindable reagent by chemical **crosslinking** means. The present invention also encompasses **conjugates** produced by this method, and methods of use of such **conjugates.** Aequorin was activated with 2-iminothiolane and then **conjugated** with **sulfo-SMCC**-activated monoclonal antibody to human TSH. The

conjugate was used in an immunoassay for TSH.
IC ICM C12Q001-00
ICS C12Q001-66
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 2
ST photoprotein **conjugate** binding reagent prepn; aequorin antibody **conjugation** TSH immunoassay
IT Ostracoda
Pelagia
(binding reagents **conjugates** with bioluminescent **proteins** of)
IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(bioluminescent, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT Aequorins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(**conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT Pharmaceuticals
(**conjugates** with photoproteins; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT Agglutinins and Lectins
Antibodies
Antigens
Hormones
Ligands
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(**conjugates** with photoproteins; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT Immunoassay
Nucleic acid hybridization
(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT Aequorins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(apo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(berovins, apo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(berovins, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)
IT Avidins

Deoxyribonucleic acids
Enzymes
Glycoproteins, specific or class
Nucleic acids
Peptides, preparation
Receptors
Ribonucleic acids
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(**conjugates**, * luminescence **binding** assays **Deoxyribonucleic** acSESEnzymesMROLES ASStGlycoproteins, speccesNucleic acids R6Peptides, preparatiD IReceptors ROLES)

IT Spectrochemical analysis
(luminescence, photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(mnemiopsins, apo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(mnemiopsins, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(obelins, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(obelins, apo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Nucleotides**, preparation
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(oligo-, **conjugates**, with photoproteins; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT **Proteins**, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(photo-, **conjugates** with binding reagents; photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 51-48-9, Thyroxine, analysis 9002-71-5, TSH
RL: ANT (Analyte); ANST (Analytical study)
(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 51-48-9D, Thyroxine, aequorin **conjugates**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 9013-20-1DP, Streptavidin, **conjugates** with photoprotein

9014-00-0DP, Luciferase, **conjugates** with binding reagents
96827-88-2DP, Pholasin, **conjugates** with binding reagents
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

IT 4856-87-5 6539-14-6, 2-Iminothiolane 6953-60-2, S-Acetylmercaptosuccinic anhydride 7803-49-8, Hydroxylamine, reactions 15209-14-0, Bis(maleimido) methyl ether 42014-51-7 55750-63-5 58626-38-3 58626-38-3D, sulfonated 64987-85-5, SMCC 68181-17-9, N-Succinimidyl-3-(2-pyridyldithio)propionate 72252-96-1 72252-96-1D, sulfonated 76931-93-6 79886-55-8 79886-55-8D, sulfonated **103708-09-4** 112241-19-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(photoprotein **conjugates** preparation and use as reagents in luminescence binding assays)

L31 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:184685 CAPLUS
DOCUMENT NUMBER: 120:184685
TITLE: Oligonucleotides having conjugates attached at the 2'-position of the sugar moiety
INVENTOR(S): Cook, Alan Frederick; Rao, Kambhampati Venkata Babaji
PATENT ASSIGNEE(S): Pharmagenics, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323570	A1	19931125	WO 1993-US4144	19930428

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1992-881255 19920511

AB An oligonucleotide wherein at least one nucleotide unit thereof is substituted at the 2'" position with a moiety -(L)n-R1, wherein L is a linker group, and n is 0 or 1; R1 is a moiety which improves uptake of the oligonucleotide into the cell and/or increases the stability of the oligonucleotide. The oligonucleotides may be employed for binding to an RNA, a DNA, a protein, or a peptide to inhibit or prevent gene transcription or gene expression, to inhibit or stimulate the activities of target mols., or the oligonucleotides may be employed as diagnostic probes for determining the presence of specific DNA or RNA sequences or proteins. Thus, glucose-attached modified oligonucleotide AGTGTTCAGTTCCGU was prepared through multiple steps by using S-Et trifluorothioacetate and 2,2'-anhydro-1-(β-D-arabinofuranosyl)uracilas starting material.

IC ICM C12Q001-68
ICS A61K031-70; C07H021-02

CC 3-6 (Biochemical Genetics)
Section cross-reference(s): 1, 9, 33

IT **Amino** acids
Carbohydrates
Dipeptides
Hormones, animal
Neurotransmitters
Peptides
Proteins

Steroids
Sterols
Vitamins
RL: RCT (Reactant); RACT (Reactant or reagent)
(**oligonucleotide modified** with, for binding
DNA, RNA, peptide and protein)

IT 51989-21-0 118849-17-5 153143-74-9 153143-74-9D, **conjugates** with long chain aminoalkylcontrolled pore glass 153835-23-5 153835-24-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of sugar-attached **oligonucleotide**, for binding to RNA or **DNA** or **protein**)

L31 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:2234 CAPLUS
DOCUMENT NUMBER: 120:2234
TITLE: Modified oligonucleotides for recognition and cleavage of RNA and their use in disease treatment
INVENTOR(S): Cook, Phillip Dan; Bruice, Thomas; Guinosso, Charles John; Kawasaki, Andrew Mamoru; Griffey, Richard
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 110
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317717	A1	19930916	WO 1993-US2057	19930305
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5359051	A	19941025	US 1992-846556	19920305
US 5514786	A	19960507	US 1992-942961	19920910
AU 9337944	A1	19931005	AU 1993-37944	19930305
JP 07502749	T2	19950323	JP 1993-515946	19930305
EP 656790	A1	19950614	EP 1993-907292	19930305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6358931	B1	20020319	US 1994-295744	19940830
AU 713740	B2	19991209	AU 1997-26244	19970624
AU 9726244	A1	19971106		
US 6232463	B1	20010515	US 1998-128508	19980804
US 2002160972	A1	20021031	US 2001-974326	20011010
US 6610663	B2	20030826		

PRIORITY APPLN. INFO.:

US 1992-846556	A	19920305
US 1992-942961	A2	19920910
US 1990-463358	B2	19900111
US 1990-566977	B2	19900813
WO 1991-US243	A2	19910111
AU 1993-38025	A3	19930225
WO 1993-US2057	A	19930305
US 1994-295744	A3	19940830
US 1997-948151	A1	19971009

AB The title modified oligonucleotides comprise an RNA cleaving moiety having at least general acid/base properties linked via an aryl or heteroaryl moiety to the oligonucleotide. The aryl or heteroaryl moiety may be an

intercalating group such as phenanthrene. The RNA cleaving moiety may be a (substituted) imidazole or bis-imidazole, or may be a structure which binds 1 or 2 metal ions. The oligonucleotide is preferably modified at the 2' hydroxyl of the sugar. The synthesis of a representative modified nucleoside, 9-((4-(7-(-5-imidazoyl-1-H)naphthyl)-O-2-propyloxy-)b-D-ribofuranosyl))adenine, was presented. This nucleoside may be incorporated into an antisense oligonucleotide to prepare a modified oligonucleotide of the invention. Methods for screening of candidate modified oligonucleotides for specificity, nuclease resistance, and RNA cleavage activity are described.

IC ICM A61K048-00
ICS C12Q001-68

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 1, 33

IT Disease
(caused by pathol. production of **protein**, treatment of, antisense **oligonucleotide conjugates** with intercalating agent and RNA-cleaving moiety for)

IT **Proteins**, biological studies
RL: PREP (Preparation)
(production of, patholog., treatment of, antisense **oligonucleotide conjugates** with intercalating agent and RNA-cleaving moiety for)

IT 58-61-7, Adenosine, reactions 106-96-7, Propargyl bromide 109-94-4, Ethyl formate 358-23-6, Trifluoromethanesulfonic anhydride 582-17-2, 2,7-Naphthalenediol 1461-22-9, Tributyltin chloride 2450-71-7, Propargyl **amine** 2537-48-6, Diethylcyanomethylphosphonate 3587-60-8, Benzylchloromethyl ether 5425-44-5, 2-Phenyl-1,3-dithiane 13528-93-3 16703-52-9, Ethyl N,N-dimethyl oxamate 18162-48-6, t-Butyldimethylchlorosilane 40615-36-9 69304-37-6, 1,3-Dichlorotetraisopropyl disiloxane 129378-52-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of **modified** nucleoside for RNA-cleaving antisense **oligonucleotides**)

L31 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:444063 CAPLUS
DOCUMENT NUMBER: 117:44063
TITLE: Antibodies to ligand analogs and their utility in ligand-receptor assays
INVENTOR(S): Valkirs, Gunars Edwin; Buechler, Kenneth Francis
PATENT ASSIGNEE(S): Biosite Diagnostics, Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 475783	A1	19920318	EP 1991-308408	19910913
EP 475783	B1	19991201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5143852	A	19920901	US 1990-583046	19900914
CA 2071904	AA	19920315	CA 1991-2071904	19910904
CA 2071904	C	20030218		
WO 9205283	A1	19920402	WO 1991-US6325	19910904
W: AU, CA, FI, JP, NO				
AU 9185361	A1	19920415	AU 1991-85361	19910904

JP 05501922	T2	19930408	JP 1991-515353		19910904
AT 187250	E	19991215	AT 1991-308408		19910913
ES 2141086	T3	20000316	ES 1991-308408		19910913
FI 9202145	A	19920512	FI 1992-2145		19920512
NO 9201864	A	19920714	NO 1992-1864		19920512
PRIORITY APPLN. INFO.:			US 1990-583046	A	19900914
			WO 1991-US6325	A	19910904

AB A competitive ligand-receptor assay uses an antibody to a ligand analog which has substantially (e.g. >100-fold) greater affinity for the ligand analog than for the target ligand. The target ligand is determined in a fluid sample by (a) contacting the sample with a ligand receptor and a ligand analog **conjugated** to a signal-generating label, such that the amount of ligand analog **conjugate** not bound to the receptor is related to the concentration of the target ligand in the sample; (b) contacting the fluid with ≥1 ligand analog antibody, so that an amount of ligand analog **conjugate** not bound to the ligand receptor is bound by the antibody; (c) contacting the fluid with a receptor capable of binding to the ligand analog antibody; (d) removing the ligand analog antibody bound to this receptor from the fluid; (e) detecting the ligand analog **conjugate** bound to the ligand analog antibody; and (f) relating the signal to the presence of amount of the target ligand in the sample. Alternative embodiments of the assay, and test devices for performing the assay, are claimed. Thus, for an assay for benzoylecgonine (I), the reaction product (II) of p-acetylthiopropionamide benzoylecgonine with sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate and aminoethanesulfonic acid was prepared and **conjugated** to alkaline phosphatase; this **conjugate** (III) was used as ligand analog **conjugate** in the assay. A sample containing I was incubated with III and a membrane-immobilized monoclonal antibody to II; the membrane was then washed and incubated with 3-indoxyl phosphate to generate a blue color in the presence of bound III. Multiple stds. were used to establish the assay response as a function of I concentration

IC ICM G01N033-53
ICS G01N033-543; G01N033-541

CC 9-10 (Biochemical Methods)

IT Deoxyribonucleic acids
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by receptor binding assay, antibody to **DNA** analog in)

IT **Proteins**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by receptor binding assay, antibody to **protein** analog in)

IT Albumins, compounds
Hemocyanins
Proteins, specific or class
RL: SPN (Synthetic preparation); PREP (Preparation)
(**conjugates**, with benzoylecgonine analog, preparation of, for benzoylecgonine immunoassay)

IT 142209-49-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with **proteins**)

IT 9001-78-9DP, Alkaline phosphatase, **conjugates** with benzoylecgonine analog
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for benzoylecgonine immunoassay)

IT **103708-09-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminoethanesulfonic acid and benzoylecgonine analog,

for benzoylecgonine immunoassay)
IT 107-35-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzoylecgonine analog and **linking** agent, for benzoylecgonine immunoassay)
IT 64987-85-5D, **protein conjugates** 103708-09-4D
, **protein conjugates**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzoylecgonine derivative)

L31 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:466230 CAPLUS
DOCUMENT NUMBER: 115:66230
TITLE: Method for coupling oligonucleotide probes with proteins
INVENTOR(S): Garman, Andrew John
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 422861	A2	19910417	EP 1990-310985	19901008
EP 422861	A3	19910925		
EP 422861	B1	20000517		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 193019	E	20000615	AT 1990-310985	19901008
JP 03290200	A2	19911219	JP 1990-277613	19901015
JP 3015445	B2	20000306		
US 5800985	A	19980901	US 1994-310057	19940922

PRIORITY APPLN. INFO.: GB 1989-23089 A 19891013
GB 1989-24822 A 19891103
US 1990-596302 B1 19901015
OTHER SOURCE(S): MARPAT 115:66230
AB Protein-labeled **DNA**, RNA, or **oligonucleotides** probes are prepared by (1) reacting the protein with a heterobifunctional linker which introduces a **thiol**-reactive group into the protein (e.g. succinimidyl 4-(N-maleimidomethyl)cycyclohexane-1-carboxylate; (2) introducing an **amino** group-containing linker into the probe, e.g. with a reagent such as **amino** link 1; (3) reacting the probe derivative with a thiolating agent such as Traut's reagent or homocysteine lactone to introduce a **thiol** group; and (4) reacting the protein derivative of step 1 with the probe derivative of step 3. The probes are easily made and offer an economic alternative to conventional radiolabeled probes. Alkaline phosphatase and horseradish peroxidase-labeled hybridization probes were prepared by the described procedure and used in hybridization assays.
IC ICM C07H021-00
ICS C12Q001-68
CC 3-5 (Biochemical Genetics)
ST **DNA** RNA **oligonucleotide protein conjugate**; hybridization probe **protein** labeling
IT **Nucleotides**, polymers
RL: PREP (Preparation)
(oligo-, **conjugates**, with **proteins**, preparation of,

simple method for)
IT **Nucleotides**, polymers
RL: PREP (Preparation)
(oligo-, deoxyribo-, **conjugates**, with **proteins**, preparation of, simple method for)
IT 1195-16-0, N-Acetylhomocysteine thiolactone 6539-14-6, 2-Iminothiolane 10593-85-8, Homocysteine thiolactone
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **amino** group-containing **oligonucleotide** derivative, protein-labeled hybridization probe preparation in relation to)

L31 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:38819 CAPLUS
DOCUMENT NUMBER: 114:38819
TITLE: Preparation of covalent conjugates of oligodeoxynucleotides and poly(amino acids) or proteins
INVENTOR(S): Westermann, Peter; Gross, Burckhard; Hoinkis, Guenter
PATENT ASSIGNEE(S): Akademie der Wissenschaften der DDR, Ger. Dem. Rep.
SOURCE: Ger. (East), 5 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 273445	A1	19891115	DD 1988-317326	19880629

PRIORITY APPLN. INFO.: DD 1988-317326 19880629
OTHER SOURCE(S): MARPAT 114:38819
AB The title conjugates are prepared by synthesizing an **oligodeoxyribonucleotide** on a carrier-bound spacer -CONH(CH2)nO2C(CH2)2CONH(CH2)nOH (n = 2-6) by the phosphoramidite method, cleaving from the carrier to provide a 3'-carboxy-**modified oligonucleotide** X-3'-OP(O)(O-)O(CH2)nNHCO(CH2)2CO2H (X = **oligonucleotide**), activating the carboxy group with e.g. 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, and condensing the product with a poly(**amino** acid) or protein. The conjugate, containing an antisense oligonucleotide complementary to a cellular or viral gene, inhibits expression of the corresponding gene in cells by hybridizing with the gene. Thus, a conjugate of 5'-CCTCACTACTTCTGGAATAGC-3' with poly-L-lysine inhibited expression of the T-antigen gene of SV40 virus in COS cells at 5-20 μM.
IC ICM C07H021-04
ICS C07K013-00; C07K015-00
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 1
ST gene expression **oligonucleotide protein conjugate**
IT **Nucleotides**, polymers
RL: ANST (Analytical study)
(oligo-, deoxy-, **conjugates**, with poly(amino acids) and **proteins**, gene expression inhibition by)

L31 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:20608 CAPLUS
DOCUMENT NUMBER: 114:20608
TITLE: Molecular sticks for controlling **protein** conformation

INVENTOR(S): Kauvar, Lawrence M.
PATENT ASSIGNEE(S): Terrapin Diagnostics, Inc., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8909233	A1	19891005	WO 1989-US1195	19890323
W: AU, BR, DK, FI, HU, JP, KR, NO, RO, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8934395	A1	19891016	AU 1989-34395	19890323

PRIORITY APPLN. INFO.: US 1988-172623 19880324
WO 1989-US1195 19890323

GI

Cys-Ala-Asp-Pro-Tyr-Glu-Glu-Gly-Asp-Asp-Gly-Arg-Thr-Cys I

AB Methods of stabilizing 3-dimensional conformations of proteins using mol. sticks are provided. A method for controlling conformation of a target peptide in solution comprises (1) providing a pair of 1st **linking** groups at designated points in the sequence of the target peptide; and (2) **conjugating** the **linking** groups to a mol. stick containing, at each and of the spacer portion thereof, a pair of 2nd **linking** groups compatible with the 1st **linking** groups. The rigid multimeric portions of the mol. sticks may be of various lengths. Proteins or peptides thus stabilized are useful in diagnosis and therapy, especially under conditions where unstabilized proteins would be denatured. Thus, mol. sticks of varying length were prepared from extension of primed oligonucleotides with Escherichia coli polymerase I and a mixture of nucleotides in which the thymidine triphosphate was derivatized to the sulfo-M-maleimido-benzoylsulfosuccinimide (**sulfo-MBS**) ester; the MBS-derivatized thymidine was capable of further reaction with sulfhydryl groups to provide thioether **linkages** to a target peptide. The peptide I, and monoclonal antibodies (MAbs) against it, were prepared with standard techniques. Samples of the peptide were reacted with the mol. sticks (Liu et al., 1979) and the restricted peptides tested for affinity to the MAb. The I50 (concentration of tethered peptide at which peptide binding is inhibited by 50%) is then plotted.

IC ICM C07K015-00
ICS C07K017-06; C07H015-12
CC 9-2 (Biochemical Methods)
Section cross-reference(s): 6
ST mol stick peptide **protein** stabilization; **nucleotide** mol stick peptide stabilization
IT Peptides, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** with mol. sticks, stability of conformation in relation to)
IT Stabilizing agents
(for peptide and **protein** conformation, mol. sticks for)
IT **Crosslinking** agents

(in mol. sticks for peptides)
IT Pharmaceuticals
Vaccines
(mimotope of, mol. sticks for **crosslinking**, stability of conformation in relation to)
IT **Proteins**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(mol. sticks for **crosslinking**, stability of conformation in relation to)
IT Amino acids, biological studies
Nucleotides, biological studies
RL: BIOL (Biological study)
(mol. sticks of, for stabilization of peptide conformation)
IT Mercapto group
(of peptide, mol. stick **linker** binding to)
IT Conformation and Conformers
(stabilization of, of peptides and **proteins**, mol. sticks for)
IT **Crosslinking** agents
(heterobifunctional, of mol. stick for stabilization of peptide conformation)
IT 365-08-2D, Thymidine triphosphate, sulfomaleimidobenzoylsulfosuccinimide esters 131060-22-5D, thymidine triphosphate derivs.
RL: ANST (Analytical study)
(in preparation of **oligonucleotide** mol. sticks for peptide stabilization)

L31 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:511968 CAPLUS
DOCUMENT NUMBER: 113:111968
TITLE: Methods, supports, and kits for multiple target analyses through nucleic acid hybridization
INVENTOR(S): Adams, Trevor H.; Schwartz, Dennis E.; Vermeulen, Nicolaas M. J.; Petrie, Charles R.
PATENT ASSIGNEE(S): Microprobe Corp., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9001564	A1	19900222	WO 1989-US3378	19890807
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				

PRIORITY APPLN. INFO.: US 1988-230066 19880809
US 1989-388202 19890804

AB Hybridization assays are provided wherein a multiplicity of different nucleic acid probes for the site-specific capture of target nucleic acids are **conjugated** to specific locations upon a single dipstick or device. The use of a dipstick has substantial mech. advantages over prior art formats for nucleic acid hybridizations. The dipsticks are composed of a handle and a nonporous support coated with a solid surface having ≥1 discrete region of nucleic acids covalently bound thereto. Also provided are means for covalently attaching nucleic acids to solid supports, improved hybridization buffers, improved support surfaces, methods for reducing nonspecific background, and methods for quantifying assay results. A multiple target dipstick for the detection of specific bacteria in patient plaque samples was prepared by immobilizing 24-mer

nucleotide species-specific sequences complementary to the hypervariable region of the 16S rRNAs from Actinobacillus actinomycetemcomitans, Bacteroides gingivalis, Eikenella corrodens, and Bacteroides intermedius in different slots on a Pall membrane derivatized with 2-aminoethanethiol. The 24-mers were synthesized possessing a 5'-terminal amine hexyl **linker**. The dipstick was placed in a sonicated solution containing lysing buffer and plaque sample, it was contacted with a solution containing biotinylated oligonucleotide universal sequence probes, and the filter was washed, reacted with streptavidin-peroxidase **conjugate**, and developed. One or all of the bacteria could be detected in a complex mixture of cells and organic material.

IC ICM C12Q001-68
CC 9-2 (Biochemical Methods)
Section cross-reference(s): 33
IT Latex
(**conjugates** with nucleic acid probes, for multiple target nucleic acid hybridization assays)
IT Immobilization, biochemical
(of nucleic acids and **proteins** on dipstick for nucleic acid hybridization assays)
IT Metals, uses and miscellaneous
RL: USES (Uses)
(on solid support for nucleic acid hybridization assay, disulfide and thiol ester **linkages** in relation to)
IT Glass, oxide
RL: ANST (Analytical study)
(**conjugates**, with nucleic acid probes, for multiple target nucleic acid hybridization assays)
IT Albumins, compounds
Caseins, compounds
Gelatins, compounds
Proteins, specific or class
RL: ANST (Analytical study)
(**conjugates**, with sulfhydryl group-containing polymer, on nucleic acid hybridization assay dipstick)
IT Coating materials
(hydrophilic, on solid support for nucleic acid hybridization assay, disulfide and thiol ester **linkages** in relation to)
IT Coating materials
(hydrophobic, on solid support for nucleic acid hybridization assay, disulfide and thiol ester **linkages** in relation to)
IT **Nucleotides**, polymers
RL: ANST (Analytical study)
(oligo-, **conjugates**, with dipstick for multiple target assay)
IT 9002-84-0D, Teflon, carboxyl group-modified, nucleic acid probe **conjugates** 9003-53-6D, Polystyrene, nucleic acid probe **conjugates** 108317-04-0D, Nytran, nucleic acid probe **conjugates**
RL: ANST (Analytical study)
(for multiple target nucleic acid hybridization assays)
IT 126601-23-8D, amine hexyl **linker** derivs., membrane **conjugates** 126601-36-3 128768-66-1 128768-67-2
RL: ANST (Analytical study)
(multiple target nucleic acid hybridization assay dipstick containing, for periodontal disease bacteria detection)
IT 60-23-1DP, 2-Aminoethanethiol, membrane **conjugates**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with modified **oligonucleotides** in preparation of hybridization dipstick)

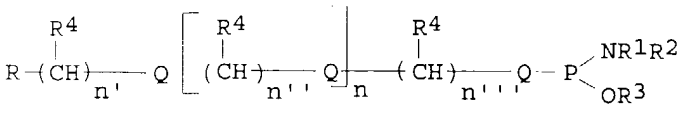
IT **106145-13-5DP**, **oligonucleotide** probe and membrane reaction products 128768-74-1DP, membrane **conjugates**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for hybridization assays)

L31 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

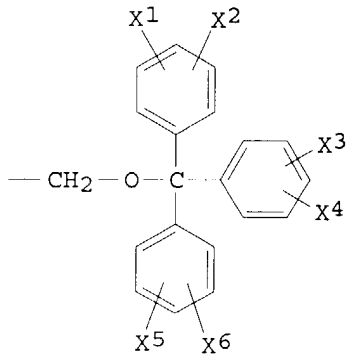
ACCESSION NUMBER: 1990:139562 CAPLUS
DOCUMENT NUMBER: 112:139562
TITLE: Phosphoramidite reagents for functionalizing **oligonucleotides** with **amine**, hydroxyl, or **thiol** groups
INVENTOR(S): Levenson, Corey; Chang, Chu An; Oakes, Fred T.
PATENT ASSIGNEE(S): Cetus Corp., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8902931	A1	19890406	WO 1988-US3212	19880919
W: DK, FI, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4914210	A	19900403	US 1987-104200	19871002
EP 380559	A1	19900808	EP 1988-908841	19880919
EP 380559	B1	19931222		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03501383	T2	19910328	JP 1988-508099	19880919
AT 98996	E	19940115	AT 1988-908841	19880919
CA 1310600	A1	19921124	CA 1988-578519	19880927
IL 87879	A1	19930610	IL 1988-87879	19880929

PRIORITY APPLN. INFO.: US 1987-104200 19871002
EP 1988-908841 19880919
WO 1988-US3212 19880919
OTHER SOURCE(S): MARPAT 112:139562
GI



I



II

AB Phosphoramidite reagents [I; R1, R2 = H, lower alkyl; R3 = β-cyanoethyl, methyl; R = protected or unprotected **amino**, **sulfhydryl**, or hydroxyl moiety; R4 = H, CH2OH or II (X1-X6 = H, lower alkyl, lower alkoxy); Q = O, NH, etc.; n, n', n'', n''' are integers] have a hydrophilic spacer arm and are suitable for introducing functional groups onto **oligonucleotides.** The reagents are more convenient to use than those of the prior art. Their synthesis and uses are described. An oligonucleotide was coupled with a tritylthio polyether phosphoramidite under standard phosphoramidite coupling procedures to yield a tritylthio oligomer. After detritylation of the oligomer it was incubated with N-maleimido-6-aminocaproyl 4-hydroxy-3-nitrobenzene **sulfonate** -derivatized horseradish peroxidase at 4 °C for 2 days. Unreacted starting materials were separated from the end-products by chromatog. The conjugate was detectable by coincidence of peaks of absorbance at 260 nm and 402 nm (heme group of peroxidase).

IC ICM C12Q001-68
ICS C07F009-24

CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 33, 37

ST **oligonucleotide protein conjugate**; **amino** group contg phosphoramidite **oligonucleotide** derivs; hydroxy group contg phosphoramidite **oligonucleotide** derivs; **thiol** group contg phosphoramidite **oligonucleotide** derivs

IT **Amino** group
Mercapto group
(**oligonucleotides** containing, preparation of, phosphoramidite functionalizing reagents for)

IT **Nucleotides**, polymers
RL: RCT (Reactant); RACT (Reactant or reagent)
(oligo-, phosphoramidite reagents for derivatization of, **amino** or **thiol** or hydroxy group containing)

IT 9003-99-0DP, Peroxidase, reaction products with maleimidoaminocaproylhydroxynitrobenzene **sulfonate**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L31 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:614504 CAPLUS
DOCUMENT NUMBER: 107:214504
TITLE: Radioactive labeling of proteins with nucleosides or nucleotides
INVENTOR(S): Dattagupta, Nanibhushan
PATENT ASSIGNEE(S): Molecular Diagnostics, Inc., USA
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4692509	A	19870908	US 1984-675373	19841127

PRIORITY APPLN. INFO.: US 1984-675373 19841127

AB A radioactively labeled protein is prepared by covalently linking the protein (e.g. insulin, Ig, protein A) to a radioactive nucleoside or **nucleotide** through an **NH2** group of the protein and a carbonyl group of a ring-opened sugar moiety of the nucleoside or **nucleotide.** The labels can be used to indicate the presence and amount of the protein in a biol. assay. 14C-labeled ATP was oxidized by treatment with NaIO4 at room temperature for 30 min. The oxidized nucleoside phosphate was adjusted to pH 8 and incubated with anti-Ig antibody for 1 h. The Schiff's base-containing product was then reduced with aqueous NaBH4. Immobilized native DNA was incubated with diluted serum samples for 1 h, washed, incubated with the labeled antibody for 1 h, and washed. The mixture was irradiated with 260 nm light in the presence of 1% SDS for 30 min to release bound DNA in solution, and the radioactivity of the mixture was counted after adding scintillation fluid. Radioactivity associated with the beads before photodecompn. or in solution after photodecompn. indicates the presence of anti-double-stranded DNA antibody and thus the presence of systemic lupus erythematosus.

IC ICM A61K043-00
ICS A61N005-12
NCL 530303000
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 8, 15
ST radiolabel **nucleotide** nucleoside **protein conjugate**; systemic lupus erythematosus RIA; Ig radiolabel oxidized ATP
IT **Proteins**, specific or class
RL: ANST (Analytical study)
(A, **conjugates**, with radiolabeled **nucleotides** or nucleosides, for bioassays)
IT Immunoglobulins
Proteins, specific or class
RL: ANST (Analytical study)
(**conjugates**, with radiolabeled **nucleotides** or nucleosides, for bioassays)
IT Nucleosides, compounds
Nucleotides, compounds
RL: ANST (Analytical study)
(labeled, **conjugates**, with **proteins**, for bioassays)
IT 7439-97-6D, Mercury, radioisotopes, uses and miscellaneous 7440-44-0D, Carbon, radioisotopes, uses and miscellaneous 7553-56-2D, Iodine, radioisotopes, uses and miscellaneous 7704-34-9D, **Sulfur**, radioisotopes, uses and miscellaneous 7723-14-0D, Phosphorus, radioisotopes, uses and miscellaneous 10028-17-8, uses and miscellaneous

RL: USES (Uses)
(nucleotides and nucleosides labeled with, for labeling proteins)

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